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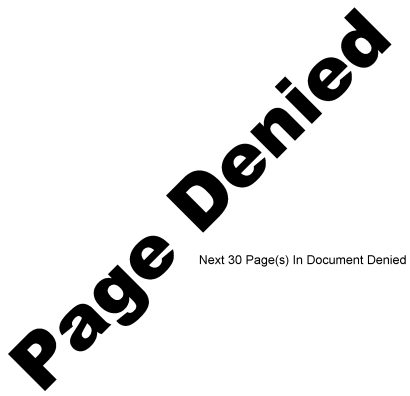

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ACADEMY OF MEDICAL SCIENCES OF THE USSR

INSTITUTE FOR POLIOMYELITIS RESEARCH

STAT

SOME RESULTS OF MASS IMMUNIZATION WITH LIVE POLIOVIRUS VACCINE IN LITHUANIAN SSR, 1959

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During all postwar years poliomyelitis was a serious problem in Lithuanian SSR. The highest incidence was registered 4 years in succession - from 1955 till 1958. A large outbreak in 1955 involved mainly Vilnius and adjoining areas. Table 1 shows poliomyelitis incidence (per 100,000 persons) by ears.

Table 1

Years									
1950	1951	1952	1953	1954	1955	1956	1957	1958	1959
1.0	3.5	3.3	4.2	2.5	15.8	12.8	6.4	10.8	2.0

The high incidence shown above and high fatality rate of this infection, reaching sometimes 6.5% (1955) or even 7.7% (1958) made us be among the first to respond to the suggestion of using new means of specific prophylaxis.

In 1957 Salk killed vaccine was used as bivaccine (type I and type III), and in 1958 as trivaccine (type I, II and III). Altogether about 59,000 children under 7 years of age received one inoculation, about 50,000 children were vaccinated twice and 20,000 children three times. Salk vaccinations were carried out in large towns and rural areas with especially high incidence. Results of these vaccinations were encouraging. For example, in Vilnius where almost 20,000 children had been vaccinated and 12,500 children revaccinated, poliomyelitis incidence was reduced from 40.0 in 1956 to 7.23 in 1958. Case-rate among the vaccinated was 4 times lower than that among the unvaccinated. In two poliomyelitis cases among the vaccinated complete recovery was reported.

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Early in 1959 on a suggestion by the Institute for Poliomyelitis Research we carried out the first trial of oral immunization about 1000 children with the live vaccine from A.B.Sabin's attenuated strains (author's lots). About half of these children had been previously vaccinated with Salk vaccine. Soon after that, observing complete areactogenicity of the live vaccine, we started large-scale immunization of the population with live vaccine prepared in Moscow at the Institute for Poliomyelitis Research. The initial plan of immunizing 500 thousand persons was exceeded. Immunization with live vaccine involved mainly children of 2 to 14 years of age inclusive, but in towns adolescents were also fed. For example, in Vilnius a portion of students and other persons under 20 years were fed.

The total number of immunized was 546,952 persons, of them 501,880 persons received all three types of vaccine and 45,072 persons - one or two types (including 2,716 persons with incomplete information).

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Table 2 - Distribution of vaccinated population in zones of Lithuanian SSR, 1959

Zone	Vaccination schedule	Estimated population under 20 years of age	Completely vaccinated persons under 20 years of age		Vaccinated children under 14 years of age	
			Number	%	Number	%
1. Vilnius and part of Kaunas zone	I-III-II	380,800	200,923	52.7	a)53,094 b)94,I09 c)4I,752	94.3 64.I 49.I
2. Kaunas city	I-(I+3+2)-(I+2+3)	74,900	40,970	54.7	29,704	60.7
3. Klaipeda zone	2 - I - 3	I64,500	82,392	50.I	76,020	56.0
4. Panevezhis zone	(I+2+3) xI	95,550	53,468	55.9	38,I7I	60.4
5. Shaulay and part of Kaunas zone	a/(I+2+3) xI	232,750	30,846	I3.2	43,868	52.9
	b/(I:2:3) x2		93,28I	46.7	5I,093	52.2
		927,500	50I,880	54.I	427,8II	58.7

a) Vilnius-city

b) Vilnius rural zone

c) Part of Kaunas zone

Among the vaccinated there were 427,811 children under 14 years of age, or 58.7 per cent of the total population in this age-group. In the age-group of 14 to 20 years there were 116,425 persons vaccinated, or 58.6 per cent of the

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population in this age group.

In different zones of the republic various immunization schedules were used (Table 2).

In Vilnius zone immunization with monovaccines was carried out according to the schedule type I followed by type III and then type II. Altogether 94,109 children up to 14 years of age, or 64.1% of the children's population, were vaccinated in this zone. In Vilnius-City immunizations involved 53,094 children under 14, or 94.3 per cent of the children's population.

Kaunas zone was divided into three parts. In 11 areas with lower incidence trivalent vaccine was used in two feedings. Altogether 43,868 children under 14 years of age, or 52.9 per cent of the children's population were vaccinated. In 9 areas with higher incidence the immunization schedule was three feedings with monovaccines of types I, III, II. The vaccine was given to 41,752 children, or 49.1 per cent of the children's population.

In the town of Kaunas, most troublesome of the whole zone, immunization of 29,704 children under 14 years of age (60.7 % of the children's population) was carried out in a reinforced schedule consisting of three feedings: first with type I followed by types I + III and then by types I + III + II.

In Shaulay zone trivalent vaccine was administrated twice, involving 51,093 children under 14 years of age, or 52.2 % of the children's population.

In Panevezhis zone one feeding with trivalent vaccine was given to 38,171 children, or 60.4 % of children under 14 years.

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In Klaipeda zone immunization was carried out with monovaccines on the schedule type II followed by type I and then type III, involving 76,020 persons, or 56 % of the children's population.

It follows from the abovesaid that in different zones immunization involved from 49.1 to 94.3 per cent of the children's population of the most susceptible age-group under 14 years.

As a result of vaccinations patterns of poliomyelitis incidence have changed sharply. Tables 3 and 4 present data for paralytic poliomyelitis since 1955, as most reliable statistically.

Table 3 - Paralytic poliomyelitis in Lithuanian SSR (by months)

Years	J	F	M	A	M	J	J	A	S	O	N	D	Total
1955	2	2	8	3	9	I5	48	78	75	49	26	I6	33I
1956	I6	6	I2	I4	II	26	27	I9	28	I6	7	7	I89
1957	7	I0	8	9	5	7	26	25	I5	6	6	7	I3I
1958	5	6	6	-	4	2I	30	45	40	25	I7	I7	2I6
1959	I0	I2	6	4	3	4x)	7	3 +)	I	2x)	I	I	54
1960	-	3	I	-									

Note: x) Of them 2 cases in June and 1 case in October, 1959, in persons over 20 years of age (unvaccinated).

+) Of them 1 case in August with doubtful diagnosis.

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Table 4 - Paralytic poliomyelitis in Lithuanian SSR

(by half-year periods)

Years	1st half-year	IInd half-year	per cent	Ratio (to 1959)
I955	39	292	82.2	292:I5=I9.5
I956	85	I04	55.0	I04:I5= 6.9
I957	46	85	64.9	85:I5 = 5.7
I958	42	I74	80.5	I74:I5 = I0.2
I959	39	I5	27.8	-

The first thing to be noted is the disappearance of the usual seasonal rise in incidence, namely, in the second half of 1959 (i.e., after vaccinations) there were only 15 cases, or 27.8 per cent of the annual paralytic poliomyelitis incidence, whereas in previous years in the second half-year period the percentage was usually from 55.0 (1956) to 82.2 per cent (1955). The largest number of cases in 1959 was in January and February (10 and 12 cases, respectively).

The ratio of the number of paralytic cases in the second half of 1959 to that for the same periods in the 4 previous years indicate a considerable reduction in postvaccination incidence (5.7 - 6.9 - 10.2 and 19.5 times lower) (see Table 4).

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Table 5 - Specified data on poliomyelitis incidence in Lithuanian SSR (by months)

Group	J	F	M	A	M	J	J	A	S	O	N	D	Total
I	I0	I2	6	4	3	4	8	5	I	2	I	I	57
II	-	-	-	-	-	-	I	2[x)]	-	-	-	-	3
III	-	-	-	-	-	2	-	-	-	I	-	-	3
IV	I0	I2	6	4	3	2	7	3[†)]	I	I	I	I	5I
V	-	-	-	I	-	I	I	I	-	-	I	I	6

Composition of groups:

I. All reported cases, including patients over 20 years of age (not vaccinated in Lithuanian SSR), and the so-called nonparalytic mild forms without laboratory confirmation.

II. Including only the so-called non-paralytic cases without laboratory confirmation.

Note: x) in this group 1 case in a live virus vaccinee (case No.50)

III. Only paralytic poliomyelitis cases in persons over 20 years of age (not vaccinated in 1959).

IV. Only paralytic poliomyelitis cases in persons under 20 years of age.

†) One fatal case in an unvaccinated person is doubtful or questionable (inadequate investigation).

V. Including paralytic poliomyelitis in persons vaccinated with live poliovirus vaccine.

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Table 5 presents specified data on distribution and characteristics of poliomyelitis cases in 1959. In the population of 0 to 20 years of age 51 paralytic poliomyelitis cases were reported in 1959, of them 35 cases before the termination of vaccine feedings and 16 cases after that. Three more cases were reported in persons over 20 years of age and 3 cases of the so-called nonparalytic forms without laboratory confirmation.

Table 6 presents data illustrating reduction in poliomyelitis incidence when the latter for 1957, 1958 and 1959 is compared by immunization zones for the second half-year periods and only for the age-group under 14 years.

Table 6 - Number of poliomyelitis cases during seven months (June-December) of 1959 compared to that in 1957 and 1958.

	1959/57	1959/58	Reduction
Vilnius City	1/20	1/14	14 times - 20 times
Vilnius zone	1/33	1/23	23 " - 33 "
Kaunas zone I	6/16	6/35	2.8 " - 5.8 "
Kaunas zone II	2/7	2/47	3.5 " - 23.5 "
Kaunas City	1/5	1/27	5 " - 27 "
Klaipeda zone	2/23	2/60	11.5 " - 30 "
Shaulay zone	-/13	-/48	13 " - 48 "
Panevezhis zone	3/5	3/18	1.6 " - 6 "

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Thus in all the zones marked reduction of incidence was observed, and in the entire republic for the seven months there was 12•5-fold reduction in incidence compared to that of 1958 and 5.4-fold reduction compared to that of 1957. The reduction is persistent now. For the first four months of 1960, according to preliminary data, 4 cases of paralytic poliomyelitis have been reported, of them two in Kaunas zone, one in Shaulay zone and one in Panevezhis zone. Three of these four patients received no vaccine, one was given one feeding with trivalent vaccine.

Effectiveness of the vaccine is indicated by the fact that of 30 children developing paralytic poliomyelitis from April, 1959 till April, 1960, 23 were unvaccinated and only 7 vaccinated. The disease in all vaccinees had a very mild course, they all had facial monoparesis and were discharged without any residual signs, with complete recovery of muscle function.

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Table 7 - Information on cases of poliomyelitis in persons immunized with live poliovirus vaccine in Lithuanian SSR.

Case No.	Age (years)	Schedule and date of vaccination	Date of onset	Diagnosis	Outcome	Results of virologic examination
33	13	Trivaccine, one feeding 6.-IV	27-IV	Monoparesis VII	Recovery	Not tested
39	5	types I-III-II 10-V, 16-VI	25-VI	-"-	-"-	No virus isolated at 17, 26 days
44	13	trivaccine, twice 8-III and 21-IV	19-VII	-"-	-"-	Not tested
48	9	types I-III-II 27-III, 27-IV, and 27-V	18-VIII	-"-	-"-	No virus isolated
56	14	trivaccine, one feeding 18-III	3-IX	*"*	-"-	-"-
57	12	type II, one feeding in March	18-XII	-"-	-"-	-"-
4	14 (1960)	trivaccine, one feeding in March, 1959	15-III-60	-"-	-"-	-"-

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One case of nonparalytic form of the disease in a child of 2.5 years of age in August, 1959, should be mentioned. This child received two feedings, first of type II and then type I monovaccine. There was no laboratory confirmation in this case.

Marked reduction in case-fatality rate was observed as a result of vaccination. For seven months of 1959, there was one fatal case in an unvaccinated child (in this case the diagnosis was also questionable).

We would like to answer the question which is of great practical importance - which of the vaccination schedules should be given priority ?

The impression is that the schedule used in Panevezhis zone (single feeding with trivalent vaccine) resulted in the least reduction in incidence. Therefore we believe that immunization should be limited to single trivaccine administration only in exceptional cases. It is probable that such immunization schedule does not provide for the adquate circulation of all three types of viruses in the community. It is particularly important for rural areas with scant population.

More satisfactory results were obtained in Shaulay zone where trivalent vaccine was administered twice. This was confirmed by serologic investigations which showed that antibody titers observed with the schedule were comparable to those after separate immunization with monovaccines.

Not quite clear is the result obtained in the first Kaunas zone where the same schedule was used. The effect here is several times lower than that in Shaulay zone, though per cent of involvement of susceptible population is the same.

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This problem requires further study.

It is possible that the decisive factor for achieving epidemiological effect lies not in vaccination schedule but in completeness of involvement. In Vilnius City, where 94.3 per cent of children's population received the vaccine the epidemiological effect is good and persistent. There have been no poliomyelitis cases from June 1959 till the present time. Nevertheless the question may probably be raised as to what minimal involvement is necessary for achieving epidemiological effect.

The data of 1959 vaccination campaign unfortunately give no answer to this question.

In March-April, 1960 revaccination with type I vaccine in dragée-candy was carried out involving more than 600,000 persons under 14 years of age, and immunization of the entire population of 0 to 60 years of age with trivalent vaccine has been started (2,000,000 persons, or up to 75 per cent of the total population of the republic).

Conclusions

1. Live vaccine prepared from Sabin attenuated strains is completely areactogenic and produces good epidemiologic effect in that marked and stable reduction in poliomyelitis incidence is achieved.

2. Single feeding with trivalent vaccine should be used only in exceptional cases, while two feedings with trivalent vaccine may be used successfully.

3. The decisive factor for sharp reduction in incidence is

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completeness of involvement of susceptible population groups.

4. The task for the near future is to determine the duration of immunity after live vaccine, on which necessity for further revaccinations will depend.

5. It is necessary also to determine the minimal percentage of coverage with vaccinations for the achievement of epidemiological effect. Immunization of total adult population may very likely be unnecessary.

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SURVEY OF THE PRESENCE OF POLYOMYELITIS ANTIBODY IN POPULATION OF DIFFERENT PARTS OF THE SOVIET UNION

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Numerous investigations on immunologic status to poliomyelitis of population in different parts of the world have shown that there exist definite differences in the process of acquisition of antibody in populations of different regions and countries. Indices of antibody prevalence in population may vary greatly.

In connection with vaccinations against poliomyelitis in the Soviet Union from 1956 to 1959 I studied poliomyelitis antibody status of population in six different regions of the Soviet Union (see Table 1).

Though blood specimen collections for the study were done in different periods we considered it possible to correlate the results obtained in different regions of the Soviet Union because these materials characterize the immunologic status before vaccination (with the killed or the live vaccine).

The study population was comprised mainly of children going to or living in children's institutions (kindergartens, nurseries, schools, children's homes), - the so-called "organized children". Only in Sverdlovsk did we survey also children not going to such institutions; these were "unorganized children".

In Estonia where before our investigation vaccinations with the killed vaccine had been carried out in some areas of the republic and later mass vaccinations with the live vaccine had been given we could study changes, related to vaccination against poliomyelitis with the killed and the live virus vaccine on large numbers of sera tested.

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In fig. 1 data on age-incidence of poliomyelitis in regions where normal population was surveyed serologically are presented. As is seen in the figure, only in Estonian SSR poliomyelitis incidence curve is extended, involving almost uniformly many age-groups, with a certain rise in the age-group of 7 to 30 years. In contrast to this, in Sverdlovsk, Ryazan, Krasnodar region and Transcarpathian region another pattern was typical - the highest incidence was observed in early childhood. These data calculated on the average for 5-7 postwar years for each study region may be considered as reflection to a certain extent, of the process of latent poliomyelitis immunization. Of course, patterns of age-distribution of poliomyelitis incidence may be related to patterns of poliomyelitis antibody in the population.

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The scale of serologic survey is shown in the Table below.

Region and year of serum collection	Total number of sera tested	of them			
		unvaccinated		vaccinated	
		organized children	unorganized children	with Salk vaccine	with live vaccine
Estonia, 1959	2,973	1,055	-	1,162	756
Sverdlovsk, 1958	985	608	377	-	-
Ryazan, 1956	1,038	1,038			
Krasnodar, 1956	525	525			
Uzhgorod, 1957	56	56			
Moscow region, 1957	42	42			
T o t a l	5,619	3,324	377	1,162	756

Sera from children were tested in pH neutralization test (Salk et al.) modified by Melnick and Opton. The initial dilution of sera was 1:2 (after addition of the virus it was 1:4). The pH test was performed in monkey kidney cell suspension, the cells being grown in bottles and treated with versene. Virulent poliovirus strains were used as antigens: type I Lugovskoy, type II Ovchinnikov, type III Leon.

Fig. 2 presents graphically the results of tests with sera from healthy children receiving no vaccinations in various parts of the Soviet Union.

The largest percentage of negative tests with poliovirus

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was obtained with sera from almost all age-groups in Estonian SSR. At the same time in Sverdlovsk, Krasnodar region, Ryazan region a large number of negative tests with all poliovirus types was obtained only in the age-group of 6 months to 2 years (80 to 100 per cent of sera). Beginning with 3 years of age the number of negative sera in these regions progressively decreases while in Estonia per cent of sera without detectable antibody to types I and III remains high till 5 years of age; also in older age-group (up to 25 years) about 30-40 per cent of persons tested had no type I and type III poliovirus antibody.

Fig. 3 presents data on "triple-negative" children (i.e., children possessing no antibody to all the three types of poliovirus). The highest percentage of such children was in the youngest age-group (1-3 years) everywhere. In Estonian SSR and Ryazan region, however, in older ages about 10% of triple-negative sera was found. Tables 1 to 5 give the results of serologic surveys in separate parts of the Soviet Union.

Fig. 4 presents graphically the results of serologic survey of the so-called organized and unorganized children in Sverdlovsk. As may be seen in the figure, there is a definite difference in per cent of sera without poliomyelitis antibody between organized and unorganized children, in that in the age-group of 6 months to 1 year the number of negative sera was higher in unorganized child ren compared to that in children going to children s institutions. Thus, in unorganized children decline of maternal immunity in the age-group of 6 months to 1 year may be noted. Apparently children going to children's

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institutions are early exposed to latent poliomyelitis infection and acquire antibody correspondingly earlier (already at the age of 6 months to 1 year) in a certain per cent of cases.

In conclusion, summary results of specific prophylactic measures in Estonia should be mentioned. These results are presented graphically in fig. 5 for three survey periods: before vaccination, after vaccination with the killed Salk vaccine and after vaccination with live poliovirus vaccine from A.B.Sabin's attenuated strains. These graphs clearly indicate sharp reduction in numbers of negative tests in serologic surveys after vaccination, especially after immunization with live vaccine.

In many age-groups there were no negative sera after live vaccine immunization, in others their number was insignificant. In total, per cent negative did not exceed 18%.

The effect of live vaccine immunization was especially marked in survey of a group of triple-negative children. While their number decreased considerably after vaccination with Salk vaccine, after live vaccine immunization it came to 0 (see fig. 6).

All these data are of certain significance for the definition of immunologic status of population with regard to poliomyelitis virus before and after vaccination.

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Table 1 - Results of tests for poliomyelitis antibody in sera from unvaccinated persons (Estonia, 1959)

Age	Total number of sera tested	% of sera without antibody to types			
		I°	II°	III°	I° II° III°
6 mo - 1 yr.	53	81	69	83	64
1	75	81	52	70	49
2	71	62	28	65	19.7
3	59	54	36	58	25.4
4	12	66	16	50	-
5	16	50	18	56	-
6	19	21	26	42	5.2
7	23	16	21	25	13
8	33	21	39	24	9
9	49	24	18	32	8
10	46	34	29	39	8.7
11	74	34	30	34	4
12	70	25	17	30	11.4
13	63	21	31	42	5.9
14	75	34	32	30	9.3
15	47	46	27	40	8.5
16	54	20	33	30	5.5
17	39	18	13	23	2.5
18	37	33	20	32	5.4
19 & 20	36	21	16	35	2.7
21	25	24	24	36	12
22	39	21	10	45	3.4
23	24	12	25	40	4.5
24 - 25	26	11	11	11	-
Total:					

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Table 2 - Results of tests for poliomyelitis antibody in sera from unvaccinated persons (Ryazan region, 1956)

Age	Total number of sera tested	% of sera without antibody to types					
		I°	II°	III°	I°	II°	III°
6 mo. - 1 yr.							
1	54	55	69.8	68		44	
2	109	50.4	58.6	58.4		35	
3	151	43.1	46.5	51.6		23	
4	58	42.1	47.3	39.6		15	
5	75	38.4	38.3	36.1		16	
6	48	40	36.1	40.4		12	
7	56	33.3	35.8	40.7		9	
8	59	31.3	35.8	38.6		6	
9	79	20.1	18.9	24.3		7	
10	68	26	23.9	33.7		7	
11	70	12.8	33.3	20.3		8	
12	34	26.4	28.9	29.4		9	
13	57	17.7	13.5	24.6		7	
14	40	12.9	11.7	12.9		-	
15	27	25.9	12.4	23		3	
16	30	13.8	13.1	24.1		6	
17	23	20	16	14.3		8	
18							
19 & 20							
21							
22							
23							
24 & 25							
Total :							

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Table 3 - Results of tests for poliomyelitis antibody in sera from unvaccinated persons (Krasnodar region, 1956)

Age	Total number of sera tested	% of sera without antibody to types					
		I°	II°	III°	I°	II°	III°
6 mo. - 1 yr.							
1	5	100	100	100		100	
2	35	59	84	71		29	
3	57	48	64	39		15.5	
4	85	36	36	31		10.2	
5	57	35	28	52		9.5	
6	45	19	41	32		4.5	
7	62	28	35	44		5.3	
8	35	31	25	26		7.4	
9	21	23	25	15		3	
10	38	19	21	30		-	
11	30	25	21	30		5.9	
12	18	28	20	6		-	
13	15	12	-	-		11	
14	20	25	15	35		7	
15							
16							
17							
18							
19 & 20							
21							
22							
23							
24 & 25							
Total:							

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Table 4 - Results of tests for poliomyelitis antibody in sera from unvaccinated persons, (Sverdlovsk, 1958).

Organized children						Unorganized children					
Age	Total number of sera tested	% of sera without antibody to types				Age	Total number of sera tested	% of sera without antibody to types			
		I°	II°	III°	I°II°III°			I°	II°	III°	I°II°III°
6 mo-1 yr.											
1	62	80	67	83	57	1	25	76	59	89	46
2	102	69	56	62	34	2	49	80	78	86	66
3	117	42	33	36	18	3	49	60	58	58	39
4	82	31	28	35	12	4	70	48	30	34	16
5	79	23	20	25	10.9	5	53	44	42	48	18
6	78	22	18	14	5.4	6	80	37	28	26	12
7	91	17	16	15	5	7	60	29	17	25	3
8	39	26	14	13	-	8	31	10	-	12	-
9						9					
10						10					
11						11					
12						12					
13						13					
14						14					
15						15					
16						16					
17						17					
18						18					
19 & 20						19 & 20					
21						21					
22						22					
23						23					
24 & 25						24 & 25					
Total:						Total:					

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ACADEMY OF MEDICAL SCIENCES OF THE USSR

INSTITUTE FOR POLIOMYELITIS RESEARCH

STAT

MATERIALS ON CONTROL OF LIVE POLIOVIRUS VACCINE IN TISSUE CULTURES DURING MANUFACTURE

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Academy of Medical Sciences of the USSR

M o s c o w

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Organization of biologic control of live poliovirus vaccine during manufacture was based on Instructions (November 10, 1958) approved by the Vaccine-Serum Committee of the Ministry of Health of the USSR and all directions by Prof. Albert B.Sabin with some additions and modifications introduced by our Institute.

Each batch and lot of the live poliovirus vaccine manufactured at the Institute for Poliomyelitis Research was, in addition to animal tests, thoroughly tested in tissue cultures.

Each batch (prior to pooling in lots) and each lot of the live vaccine were subjected to the following tests in tissue cultures:

1. Determination of the titer of vaccine virus in the liquid vaccine and dragée-candies with vaccine (live vaccine potency test).

2. Identification of the vaccine virus.

3. Test for the absence of B virus in vaccine;

4. Test for the absence of measles virus in vaccine;

5. Test for the absence of spontaneous simian viruses in vaccine.

All these tests were performed by the following methods.

1. Determination of vaccine virus titers:

(a) in the liquid vaccine was done in roller tube cultures of 7-day old trypsinized monkey kidney cells and by the plaque method. Each batch of the live vaccine before pooling into a lot was tested at 36°C and 40°C, two tubes per dilu-

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tion in 1 log steps. 0.2 ml of respective dilution and 1.8ml of medium 199 were added into each tube. Results were read at 7 days. (Results of this part of the control work are presented in communication by Shmeleva, G.A.).

Pooled batches of the live vaccine were titrated in roller tube cultures at 36°C. Dilutions were prepared by 0.5 log steps. 10 tubes were taken per dilution, each tube being inoculated with 0.2 ml of respective dilution and 1.8 ml of medium 199. Results were read also at 7 days, the titer calculated by the method of Reed and Muench. The number of TCD_{50} in 1 ml of the vaccine was determined.

Besides, lots of the live vaccine were selectively titrated by the plaque method (modified by Hsiung and Melnick). For these tests 250 ml bottles with 7 day cultures of trypsinized monkey kidney cells (area of cell monolayer = 60 cm^2) were used. For titrations by the plaque method vaccine dilutions $10^{-5.0}$ or $10^{-5.5}$ were usually prepared. These dilutions were inoculated into 2-3 bottles (0.2 ml per bottle). Plaque counts and estimation of the number of PFU per 1 ml. of the vaccine were done at 5-6 days.

(b) Determination of vaccine virus titer in dragée-candy.- All lots of the vaccine produced in the form of dragée-candy were tested for virus titer in individual candies by the plaque method.

Titration of the pool of 100 candies from each lot of the vaccine. 100 dragée-candies (average weight of 1 gm each) were solved in 400 ml. of Hanks' solution with antibiotics (penicillin and streptomycin, 1000 units/ml, each). This

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dilution of candies (1/5) was further diluted 1/50, 1/200 and 1/800. Each dilution was inoculated into 3 to 10 250 ml. bottles (0.2 ml. per bottle) with 7-day cultures of trypsinized monkey kidney cells (area of cell monolayer = 60 cm^2). After 1 hour of adsorption at 36°C all bottles were overlayed with agar according to prescription by Hsiung and Melnick ($NaHCO_3$ concentration = 0.66% per ml). Bottles inoculated with liquid live vaccine used for manufacture of dragée-candy being tested served as control (the liquid vaccine was used for inoculation of bottles in $10^{-5.0}$ to $10^{-5.5}$ dilution). Results of titration were read at 5-6 days.

Titration of 10 individual dragée-candies of each lot of the vaccine.

Each candy was diluted in 9 ml of Hanks' solution. Bottles were inoculated also with 1/50, 1/200 and 1/800 dilutions; each dilution (0.2 ml per bottle) was added into two bottles with 7-day cultures of trypsinized monkey kidney cells and left for adsorption for 1 hour at 36°C.

Control bottles were inoculated with liquid live vaccine used for manufacture of the dragée-candies being tested. Agar overlay was used as mentioned above. Results were read at 5-6 days.

2. Identification of vaccine virus was done against potent hyperimmune homotypic rabbit sera. Antisera against types I, II and III polioviruses were used in 1/10 and 1/50 dilutions. 100 TCD_{50} of virus in 0.25 ml was added to 0.25 ml of serum dilution. Virus-serum mixtures were kept at 36° - 37°C for 1 hour, and then 0.2 ml aliquots were added into each of

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two tubes with 7-day culture of trypsinized monkey kidney cells. 1.8 ml of medium 199 were added to each tube. Inoculated cultures were observed for 14 days, with change of the medium at 7 days. Control tubes were inoculated with serum alone, virus alone and medium 199 (without either virus or serum).

3. Tests for the absence of B virus in vaccine were carried out in trypsinezed rabbit kidney cell cultures (from rabbits of 2-3 week old). 7-10-day cultures of rabbit kidney cells grown in medium 199 in 250 ml bottles (area of cell monolayer = 60 cm^2) served as controls. Two bottles were inoculated each with 10 ml of vaccine lot tested and 40 ml of medium 199 or Eagle's medium. One bottle was inoculated with 0.5 ml of undiluted culture fluid containing B virus with the objective to test sensitivity of the cells to B virus. Two bottles were left uninoculated in order to rule out spontaneous degeneration of the cells (only 50 ml. of fresh medium were added to these bottles). All bottles were observed for 14 days, with change of medium at 7 days. Bottles inoculated with B virus were discarded immediately after development of complete degeneration of the cells.

4. Tests for the absence of measles virus in vaccine were performed in trypsinized dog kidney cell cultures (kidneys from 2-4 months old dogs were trypsinized) or in trypsinized human amniotic cell cultures. Trypsinized dog kidney cells were grown in medium 199 with 5% calf serum, and amniotic cells were grown in medium 199 with 20% calf serum.

For tests of each batch (lot) of vaccine 10 tubes of the mentioned tissue cultures were used (7-day cultures of dog

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kidney cells or 7-10-day cultures of human amniotic cells).

In tests for the absence of measles virus 1 ml of undiluted vaccine being tested was mixed with 1 ml of undiluted potent rabbit serum of the respective type, that is, type I virus was mixed with type I serum, type II virus with type II serum and type III virus with type III serum (in tests homotypic sera were used obtained from rabbits immunized with virulent poliovirus strains which had been propagated in continuous cultures of cynomolgus heart cells. Sera with titers not less than 1:3000 - 1:6000 were used). Serum-virus mixture was kept for 1 hour at 36°C, and then aliquots of 0.2 ml were inoculated into each of 10 tube cultures of trypsinized dog kidney cells or 10 tube cultures of amniotic cells. 1.8 ml of medium 199 were added into each tube. Inoculated cultures were observed for 21 days with change of medium at 7 and 14 days. 10 tube cultures of each cells were left uninoculated for control of spontaneous degeneration of the cells.

5. <u>Tests for the absence of spontaneous simian viruses in vaccine</u> were carried out in two stages. In the first stage initial uninoculated kidney cell cultures comprising up to 10-25% of total number of cultures obtained from each pair of kidneys and selected for control were observed for 21 days. On appearance of suspect spontaneous degeneration of cells in these cultures corresponding batches of vaccine were discarded irrespective of whether the specificity of these changes could be confirmed, and were no longer subjected to other tests.

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In the second stage tests for the absence of spontaneous simian viruses in batches of vaccine prior and subsequent to pooling in lots were done by neutralization tests with potent hyperimmune rabbit sera in monkey kidney cell cultures. The technique of these tests was similar to that in tests for the absence of measles virus (see item 4).

Results of vaccine control

1. Determination of virus titers in liquid live vaccine indicated that the vast majority of vaccine lots contained from 5 to 20 million plaque-forming units of the virus per 1 ml.

Results of titration of vaccine virus in lots of live vaccine released during 1959-1960 are given in Table 1.

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Table 1 - Titers of vaccine virus in live poliovirus vaccine lots

Lot No.	Type of virus	Titer per 1 ml in TCD_{50}	Titer per 1 ml in PFU
0	I	50.12×10^6	
0	II	89.13×10^6	
0	III	50.12×10^6	
I	I	39.81×10^6	
2	II	67.61×10^6	
3	III	16.60×10^6	
4	II	25.12×10^6	
5	I, II, III	consists of vaccine lots No. I, 2 and 3	
6	III	28.18×10^6	
7	II	15×10^6	
8	I	13.6×10^6	
9	I	11.4×10^6	
10	I	10.4×10^6	
11	II	12.2×10^6	
12	II	11.3×10^6	
13	II	11×10^6	
14	III	11.8×10^6	
15	III	11.9×10^6	
16	I, II, III	consists of vaccine lots No. 8, II and I4	
17	II	19×10^6	
18	III	75.9×10^6	
19	II	13.8×10^6	
20	I	21.4×10^6	
21	I, II, III	consists of vaccine lots I7, I8 and 20	
22	I	4×10^6	
23	I	3.4×10^6	
24	I	4×10^6	
25	I	4×10^6	21×10^6
26	III	19.5×10^6	
27	III	12.9×10^6	

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Table 1 - Titers of vaccine virus in live poliovirus vaccine lots (continued)

Lot No.	Type of virus	Titer per 1 ml in TCD_{50}	Titer per 1 ml in PFU
28	III	6.2×10^6	20.1×10^6
29	III	12.9×10^6	
30	II	6×10^6	
31	II	8.4×10^6	7.3×10^6
32	III	22.4×10^6	
33	II	8.9×10^6	
34	III	10×10^6	
35	I	8.3×10^6	
36	II	7.6×10^6	
37	II	5.6×10^6	
38	I	6.6×10^6	
39	III	18.6×10^6	12.3×10^6
40	II	7×10^6	6.8×10^6
41	I	3.2×10^6	14.1×10^6
42	I	7.9×10^6	4.8×10^6
43	I	8.9×10^6	8.1×10^6
44	I	5.3×10^6	11.4×10^6
45	I	17.4×10^6	13.2×10^6
46	I	11.5×10^6	12.3×10^6
47	I	17.4×10^6	9.5×10^6
48	I	10.2×10^6	15.4×10^6
49	III	21.9×10^6	14.8×10^6
50	III	12.9×10^6	13.2×10^6
51	III	9.1×10^6	13.5×10^6
52	II	4×10^6	14.7×10^6
53	II	12.9×10^6	13.5×10^6
54	I	11.2×10^6	19.5×10^6
55	II	11.2×10^6	12.3×10^6
56	I	8.7×10^6	
57	III	8.2×10^6	
58	III	8.7×10^6	
59	I	10×10^6	

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Table 2 shows examples of titration of three liquid live poliovirus vaccine lots in tube tissue cultures.

Table 2 - Titration of live poliovirus vaccine (selective protocols of February and March, 1960)

Virus dilutions	Vaccine lot No. and virus type		
	No.47 Type I	No 53 Type II	No.50 Type III
$10^{-4.5}$	10/10	10/10	10/10
$10^{-5.0}$	10/10	10/10	10/10
$10^{-5.5}$	10/10	10/10	10/10
$10^{-6.0}$	7/10	10/10	10/10
$10^{-6.5}$	1/10	4/10	4/10
$10^{-7.0}$	0/10	0/10	0/10
$10^{-7.5}$	0/10	0/10	0/10
$10^{-8.0}$	0/10	0/10	0/10
titer in TCD_{50} per 1 ml	$10^{7.24}$	$10^{7.11}$	$10^{7.11}$

Note: Numerator - number of tubes with 4 + degeneration of cells.

Denominator - total number of inoculated tubes.

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It should be pointed out that selective titration of live vaccine lots by the plaque method (see Table 1) revealed some discrepancy in titration results compared to those by tube test maximum by 0.5 - 0.6 log higher or lower, i.e. within the standard error.

Calculation of vaccine virus content in dragée-candy and control of titers in dragée

Variations in live vaccine titers were taken into account when the vaccine was manufactured in the form of dragée-candy. Lots of live vaccine containing less than $10^{7.0}$ TCD_{50} ($10x10^6$ plaque-forming units) were used for candied vaccine manufacture, with increase of the quantity of liquid vaccine per 1 kilo of candy mass. For example, if the liquid vaccine had a titer of 10 million PFU or greater, 10 ml of vaccine were taken per 1000 dragée-candies, while with the titer of the vaccine being 2 to 5 million PFU, from 20 to 60 ml of vaccine was taken per 1000 pieces of dragée. If trivalent or bivalent mixture of monovaccines was manufactured, up to 60 ml of vaccine was taken per 1000 pieces of dragée (10-20 ml of each type). Most of dragée-vaccine lots were manufactured at a rate of 10 ml per 1000 pieces of dragée, or at least 100,000 PFU per 1 dragée. Table 3 illustrates these calculations.

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Table 3 - Calculations for the addition of vaccine virus per 1 kg (1000 pieces of dragée) depending on the virus titer

Titer per 1 ml	Absolute number of TCD_{50} or PFU per 1 ml	Amount of vaccine added per 1000 pieces of dragée	Estimated (theoretical) number of TCD_{50} or PFU per 1 dragée
$10^{6.5}$	3,162,000	30	94,860
$10^{6.8}$	6,310,000	20	126,200
$10^{7.0}$	10,000,000	10	100,000
$10^{7.1}$	12,520,000	10	125,900

Tests for the live poliovirus content in dragée-candies were made by the plaque method with the above-mentioned modifications (determination of virus content in each of 10 dragée-candies and in a pool of 100 pieces of dragée).

Tables 4 and 5 illustrate the results of virologic control of one of ordinary candied vaccine lots. Distribution of the vaccine virus in individual candies was uniform, as a rule (variations ± 50% of the estimated dose of 100,000 PFU). It should be taken into account that under conditions of dragée-candy manufacture in boilers variations in the weight of individual pieces in the range of ± 15% are possible, which is not very significant.

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Table 4 - Titration of candied live poliovirus vaccine (dragée) by the plaque method (from a pool of 100 dragée-candies).

Virus type	Virus lot No.	Liquid vaccine titer in PFU	Date of dragée manufacture and amount of virus per 1000 candies	Conditions of storage of dragée candy	Dilution of dragée or control	Bottles No	Number of plaques	Average number of plaques per 1 bottle	Number of PFU per 1 dragée-candy
III	51	13.5×10^6	7.IV 1960 10 ml	6 days at - 20°C	1/50	1 2 3	confluent growth of plaques	not counted	
III	51	13.5×10^6	7.IV 1960 10 ml	6 days at -20°C	1/200	1 2 3	116 125 146	129	129,000 (129×10^3)
III	51	13.5×10^6	7.IV 1960	6 days at -20°C	1/800	1 2 3	36 48 52	45.3	181,200 (181.2×10^3)

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Table 5 - Results of titration of candied live poliovirus vaccine (dragée) by the plaque method (for individual dragée). Type III vaccine, lot No.51, titer 13.5×10^6, 10 ml per 1000 dragée-candies. Inoculation with 0.2 ml of 1/800 dilution per bottle.

Dragée No.	Number of plaques in bottles	Average number of plaques per bottle	Number of PFU per 1 dragée-candy
1	22.26	24	96×10^3
2	24.24	24	96×10^3
3	26.24	25	100×10^3
4	56.43	49.5	198×10^3
5	24.28	26	104×10^3
6	49.34	41.5	166×10^3
7	26.30	28	112×10^3
8	19.28	23.5	94×10^3
9	37.42	39.5	158×10^3
10	22.30	26	104×10^3

The data presented in these tables do not significantly differ from titration results for other lots of candied vaccines. Since the data of experimental control of the candied vaccine will be reported in a separate communication, we shall not discuss this part of work at greater length. Routine titration of further lots of dragée-candies with live vaccine as well as experimental trials of its establishment and immuno-

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genicity (Fleer, G.P., Voroshilova, M.K., Taranova, G.P.) demonstrated advisability of using the candied vaccine. Every-day control of manufactured lots of candied vaccine also confirmed acceptability of technological directions for dragée-candy production developed by Prof. A.A.Bezzubov. Virus content in different candies of the same lot met the approved "Technical Requirements" though it varied to a certain extent (variations of ± 50% of the estimated number of PFU in the vaccine taken per given lot are allowed), but the virus content in one candy never exceeded that in others more than by 0.5 log (that is, it was within the standard error of the current titration methods).

3. Tests for identification of vaccine virus in batches and lots of live poliovirus vaccine showed in all cases that the virus type in released vaccine lots corresponded to that of seed virus used for its manufacture.

Table 6 presents a protocol of a standard test for vaccine virus identification in tube tissue cultures.

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Table 6 - Protocol of a test for live vaccine virus identification (for procedure of the test see "methods")

Vaccine lot No. and type	Type I serum		Type II serum		Type III serum		Mixture of types I,II,III sera
	1:10	1:50	1:10	1:50	1:10	1:50	1:10
No.47 Type I	0/2	0/2	2/2	2/2	2/2	2/2	0/2
No.53 Type II	2/2	2/2	0/2	0/2	2/2	2/2	0/2
No.50 Type III	2/2	2/2	2/2	2/2	0/2	0/2	0/2
Serum control (without virus)	0/2	0/2	0/2	0/2	0/2	0/2	0/2

Note: Working virus dilution in this experiment is 10^{-4}.
Numerator - number of tubes showing degeneration
Denominator - total number of tubes inoculated.

4. Tissue culture tests for the absence of B virus in the vaccine in all cases gave quite favourable results: not a single lot of live poliovirus vaccine contained B virus, in tests carried out from January 1959, to April, 1960. Table 7 presents one of the protocols of tests for B virus in live poliovirus vaccine.

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Table 7 - Protocol of a test for B virus in live poliovirus vaccine. (Trypsinized rabbit kidney cell cultures in 250 ml bottles)

Material tested	Dose inoculated	Eagle's medium	Date of inoculation	Results of 14-day observations
Live vaccine lot No.50 type III	10 ml	40 ml	11.III.60	0
Live vaccine lot No.50 type III	10 ml	40 ml	11.III.60	0
Medium without virus	-	50 ml	11.III.60	0
Medium without virus	-	50 ml	11.III.60	0
Undiluted B virus	0.5 ml	49.5 ml	11.III.60	4

Note: 0 = no cell degeneration
4 = 4+ cell degeneration.

5. Results of control for latent simian viruses. All batches and lots of live poliovirus vaccine released were found in tissue culture tests to be free from nonpoliomyelitis cytopathogenic agents including measles virus and latent (spontaneous) simian viruses. Table 8 presents results of one such test with live vaccine for nonpoliomyelitis cytopathogenic agents.

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Table 8 - Protocol of a test with live poliovirus vaccine for the absence of contamination with nonpoliomyelitis cytopathogenic agents.

Live vaccine lot and type	Amount of undiluted virus	Type, number and titer of immune serum	Number of tubes and amount of inoculum	Results
No.47, type I	1 ml	Type I serum, No.793; 1/37, 400	10 tubes 0.2 ml	0/10
No.53 type II	1 ml	Type II serum, No.795 1/8,000	10 tubes 0.2 ml	0/10
No.50 type III	1 ml	Type III, serum, No.497 1/8,000	10 tubes 0.2 ml	0/10

Note: 0 = no degeneration in inoculated tubes.

All tissue cultures used for propagation of vaccine polioviruses were carefully observed in order to rule out contamination with spontaneous simian viruses. From 10 to 25% of uninoculated tissue cultures obtained from each pair of trypsinized kidneys were kept for 21 days for detection/multiplication of spontaneous simian viruses. If any slightest signs of cell degeneration appeared in these cultures, corresponding batches of vaccine were discarded.

Tests by passages of several samples from cultures with spontaneous degeneration were made with the only purpose to find out exact causes of degeneration and did not influence

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the decision of discarding such cultures. These tests far from always ended with typing of spontaneous simian viruses (because of the lack of reference sera). For the last 6 months tissue cultures obtained from trypsinized kidneys of 604 monkeys underwent such tests. Of the total 20,578 tissue cultures grown in 1.5 litre bottles about 300 tissue cultured were suspected of being contaminated with spontaneous viruses (1.45 - 1.7 per cent of total number of tissue cultures used in vaccine manufacture). In two cases spontaneous degeneration was of "foamy" nature, in three cases there was "lacy" cell degeneration. But in the great majority of discarded tissue cultures there was vacuolization of cell monolayer with areas of detachment of cells from the glass which is similar to degeneration caused by a virus described by Hull and Minner together with other spontaneous simian viruses. It should be emphasized that not in a single instance of finished vaccine control have we found any spontaneous viruses. During the last 6 months we encountered two cases of microfilarial isolation from trypsinized monkey kidney cultures (0.3 per cent of the number of monkeys used for vaccine production). Cultures contaminated with filariae were always discarded. The possibility of penetration of filariae into kidney cell cultures confirms the necessity of retaining filtration of live poliovirus vaccine through asbestos filters impassable for filariae.

Conclusions

1. One-and-a-half year experience of biologic control of live poliovirus vaccine during manufacture (179 batches,

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52 lots, altogether over 4,000 litres) and successful use of this vaccine have demonstrated complete acceptability of biologic control requirements suggested by A.B.Sabin and used in the USSR with some slight additions and modifications.

2. Apprehensions often expressed about possible difficulties in live vaccine manufacture due to contamination with spontaneous simian and other extraneous viruses have proved to be exaggerated. Observance of a certain technological regimen in manufacture and requirements of biologic control helps to avoid serious impediments in manufacture of live poliovirus vaccine. We consider it necessary, however, to improve and simplify methods of live vaccine testing for the absence of contamination with extraneous viruses.

3. Potency tests with live vaccine in the form of dragée-candy demonstrated great uniformity of virus content in dragée-candies of various lots and good preservation of vaccine virus in dragée at different temperatures.

Every-day control of ordinary lots of candied vaccine (dragée) showed that during mass vaccination program of 1960 involving over 60 million people vaccine with quite satisfactory titers was used, the candy form being very convenient for mass administration. Results of biologic control tests confirm the acceptability of Technical Requirements and Technological Directions for live poliovirus vaccine in dragée-candy manufacture.

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INVESTIGATION OF TYPE III POLIOVIRUS STRAINS, RECOVERED FROM LIVE VIRUS VACCINES, IN MONKEY TESTS AND BY TITRATIONS AT 36°C and 40°C

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Balayan, M.S., Tolskaya, E.A.

M o s c o w

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The problem of possible reversion of pathogenic properties in attenuated strains is of the utmost importance under conditions of vaccination carried out in summer when increased dissemination of "wild" poliovirus strains occur and, consequently, some increase of neurovirulence of attenuated strains might be expected.

In the present study several type III isolates recovered from stools of children at various times after feeding with trivalent live vaccine from Sabin strains were tested.

Materials and methods

Vaccination was performed with the mixture of strains of the three types (lots No.1, 2, 3), 100,000 TCD_{50} each. Isolation and typing of strains was done in monkey kidney tissue cultures.

As a rule, type III strains alone, without admixture of types I and II strains, were recovered only from older children possessing antibody to all three poliovirus types. Table 1 lists the information on children from whom test viruses were isolated.

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Table 1 - Information on children yielding strains tested by intracerebral inoculation in rhesus monkeys and for the capacity to multiply at 36°C and 40°C.

Name	Age (years)	Antibody	Duration of type III strains excretion in stools
Shev. T	13	+++	5 weeks
Sur. S.	12	+++	4 -"-
Kam. V.	14	+++	5 -"-
Dem. Yu.	9	+++	5 -"-

Type III poliovirus was regularly isolated from these children during 4 to 5 weeks. For tests two strains from each child were selected: one isolated during first 3-10 days, and the other isolated 21 to 30 days after vaccination. For monkey inoculation and titration tissue culture fluid of the first passage was used.

Rhesus monkeys weighing 1.7 - 2.7 kilos were inoculated with 0.5 ml into each thalamus . 24 hours later the monkeys were examined for signs of brain tissue trauma. After that the monkeys were observed for 28 days at which time they were sacrificed for virologic and histologic examination which was performed in the Laboratory of Pathomorphology, Institute for Poliomyelitis Research by I.A.Robinson, M.A.Sheftel, A.P.Savinov, M.P.Frolova and A.L. Yurovetskaya.

Virus isolates were titrated in tube cultures of monkey

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kidney tissue incubated at 36°C and 40°C. Parallel titrations under similar conditions were performed with vaccine Leon $12a_1b$ strain and Mahoney strain. Titers were calculated by the method of Reed and Muench. The difference of titers at 36° and 40°C (EOG = efficiency of growth) of a test strain was divided by that of Leon $12a_1b$ strain and in this way a ratio of T-character of a strain was determined. Attenuated strains (T-) had an EOG ratio to Leon $12a_1b$ greater than 0.75; strains with lower degree of attenuation (T ±) had an EOG ratio to Leon $12a_1b$ of 0.30 to 0.75, and virulent strains (T +) had an EOG ratio to Leon $12a_1b$ below 0.3 (after Bengesh-Melnick).

Results

Inoculation of monkeys with either $10^{6.5}$ TCD_{50} or $10^{5.5}$ TCD_{50} of two strains recovered from child Shev. on the 3rd and on the 30th day after vaccination did not produce any clinical signs of poliomyelitis (Table 2). Histologic lesions were found in two monkeys, one inoculated with $10^{5.5}$ TCD_{50} of the strain isolated on the 3rd postvaccination day, and the other inoculated with $10^{5.5}$ TCD_{50} of the strain recovered on the 30th postvaccination day. It is noteworthy that one of the monkeys showed high muscle tone of the left leg 24 hours after inoculation.

Monkeys inoculated with strains isolated on the 3rd and on the 21st postvaccination day from child Sur. did not develop disease either. One of the monkeys inoculated intracerebrally with $10^{7.3}$ TCD_{50} of the strain isolated on the 21st post-

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vaccination day exhibited histologic lesions typical of non-paralytic poliomyelitis.

On inoculation with Kam. strain isolated on the 10th postvaccination day, one monkey receiving $10^{6.5}$ TCD_{50} intracerebrally developed paralysis of the lower extremities 28 days after inoculation. Monkeys inoculated with $10^{5.5}$ TCD_{50} of the virus showed neither clinical nor histological signs of poliomyelitis.

Four monkeys inoculated with a strain recovered from the same child on the 30th postvaccination day exhibited no clinical symptoms of poliomyelitis. Histological examination, however, showed lesions typical of poliomyelitis in two monkeys inoculated with $10^{6.3}$ and $10^{5.3}$ TCD_{50}. It should be said that one of these monkeys had transitory high muscle tone of the right leg 24 hours after inoculation, and another had reduced muscle tone of the lower extremities and reduced patellar reflexes which indicated brain trauma on inoculation.

Thus, of 29 monkeys inoculated with six strains isolated from vaccinated children, clinical signs of the disease were observed in one monkey inoculated with Kam. strain recovered on the 10th postvaccination day.

Histological examination the detailed results of which are presented in a report by Robinson, I.A., Sheftel, M.A., Frolova, M.P., Savinov, A.P. and Yurovetskaya, A.L., showed typical poliomyelitis lesions in one of the five monkeys inoculated with four of the six strains.

Five monkeys inoculated with Sur strain isolated on the 3rd postvaccination day exhibited no histologic lesions.

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Histologic lesions were found in two of the four monkeys inoculated with Kam. strain isolated on the 30th postvaccination day.

Consequently, strains isolated from vaccinated children, especially Kam. strains isolated on the 10th and on the 30th postvaccination days, possessed somewhat higher intracerebral activity compared to that of type III vaccine strain. No correlation between the increase of intracerebral activity of strains and duration of multiplication in the human intestinal tract was observed.

Study of T character of type III strains, recovered from children Sur., Shev., Kam. and Dem. demonstrated that they belonged to T - strains (T character ratio was 0.88 to 1.21).

Conclusions

1. On intracerebral inoculation of rhesus monkeys with type III strains isolated from stools of vaccinated children some increase of neurovirulence was observed compared to that of type III vaccine strain, lot No.3.

2. By the capacity to multiply at $36^{\circ}C$ and $40^{\circ}C$ all new isolates belonged to attenuated T – strains.

3. Some increase in intracerebral activity of the above strains, considering their complex characteristics, cannot be regarded as true reversion of type III attenuated poliovirus strain to pathogenic properties.

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Table 2 - Intracerebral activity of type III poliovirus strains recovered from children during first 10 days and 3 to 4 weeks after vaccination with trivalent live vaccine from Sabin strains

Strain	Time after vaccination	Log_{10} TCD_{50}	Results of clinical observation	Results of histologic examination	Slight trauma 24 hours after inoculation
Shev.	3 days	6.5	0 0 0	0 0	
		5.5	0 0 0	0 0 +	
Shev.	30 days	6.5	0 0 0	0 0 0	
		5.5	0 0	0 +	slight trauma
Sur.	3 days	7.0	0 0	0 0	
		6.0	0 0 0	0 0 0	
Sur.	21 days	7.3	0 0 0	0 +	
		6.3	0 0	0 0	
Kam.	10 days	6.5	0 28	0 +	
		5.5	0 0	0 0	
Kam.	30 days	6.3	0 0	0 +	slight trauma
		5.3	0 0	0 +	slight trauma

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Table 3 - Temperature characteristics of type III poliovirus strains isolated from children during first 10 days and 3 to 4 weeks after vaccination with trivalent live vaccine from Sabin strains

Strain	Time after vaccination	Log TCD$_{50}$ at 36°C	Log TCD$_{50}$ at 40°C	Difference (EOG)	EOG difference for Leon 12 a_1 b strain	Ratio of T character	Strain character
Shev.	3 days	6.5	0	6.5	6.0	1.08	T-
Shev.	30 "	6.3	0	6.3	6.0	1.05	T-
Sur.	3 days	7.0	0	7.0	6.0	1.17	T-
Sur.	21 "	7.3	0	7.3	6.0	1.21	T-
Kam.	10 days	6.5	0	5.5	6.0	0.92	T-
Kam.	30 "	6.3	1.0	5.3	6.0	0.88	T-
Dem.	3 days	6.65	0	6.65	6.0	1.11	T-
Dem.	30 "	7.0	1.5	5.5	6.0	0.92	T-

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The determination of the dosage of vaccine for the type I /CHAT/ and the type III /Fox/

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Preliminary Communication

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In connection with the preparation of the vaccination campaign in Poland, studies were inaugurated regarding the immunising properties of the vaccine, depending on the dose introduced inzo the organism.

The investigation was conducted in a Home for Children. 37 children aged 6 months to 3 years were taken into account. The examination of the specimens of stool and blood were carried out before the administration of the vaccine. Then, the living attenuated strains of Koprowski type 1 /CHAT/ have been administered orally; the following dosage was used - 1 000 000, 200 000 and 100 000 $TCID_{50}$. Subsequently specimens of stool were collected from the vaccinated children after a 3, 7 and 30 days. Specimens of blood were also collected again after 30 days.

At the same time i.e. 30 days after the first vaccination /type 1 CHAT/ a second dose of the living attenuated Koprowski strein type 3 /FOX/ was given to the same children. The dosage amounted to 200 000 and 100 000 $TCID_{50}$. The second vaccination was followed by the collection of specimens of stool 3 and 7 days after administration of type 3 vaccine. Blood was also examined for a second time after 30 days. The last blood control test was performed 3 1/2 months after the administration of the type 1 virus.

The results of the sirusological examinations are given in the table Nr 1.

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Table Nr 1

Out of the 37 children examined before vaccination presence of the Polio virus type 1 in stool was ascertained in 4 cases. However, prior to vaccination no antibodies against the virus Polio type 1 have been detected in the above named cases. One might suppose that we had to deal with a fresh, symptomless infection, and that the antibodies have not been produced, as yet.

The table indicates that the highest percentage of isolated virus strains was obtained with the dosage 1 000 000 $TCID_{50}$. on the other hand a lower percentage was obtained when the dosage amounted to 200 000, finally the lowest one after the application of 100 000 doses.

In general, irrespectivelly of the dosage, the virus type 1 has been isolated in 80%. It should be added that in 2 cases neither the isolation of the virus nor the increase of antibodies could be demonstrated.

In a certain number of cases the virus type 1 was isolated after 30 days.

The results obtained after the vaccination with the virus type 3 are similar to those arrived at with the virus type 1. In all, the virus has been isolated in 76%.

It should be indicated that the isolation of the virus was attempted 3 and 7 days after vaccination, if the period of study should be lenghtened the percentage of positive findings would probably be much higher.

As a result of our investigations we could ascertain that the viruses used for vaccination, have definite affinity to

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the intestinal tract, and can multiply there. The vaccine administered to children - in the dosage, named above, - produced no symptoms of the disease.

Serological examinations performed prior to vaccination, indicated that with the exception of three children, no child in the group had antibodies against the 3 types of the Polio virus.

The antibodies concentration in 2 children amounted to 1/8 for the types 1 and 3, and that for the type 2 to 1/4. In the third child the concentration of antibodies for the type 1 only, was 1/8.

The results of the blood examination following vaccination are given in the table Nr 2.

Table Nr 2

The table shows that the antibodies against type 1 showed the highest increase after 110 days. No antibodies have been detected in 16% of children, i.e. that in 84% the presence of antibodies has been proved, and antibodies in the concentration from 1/16 to 1/1024 appeared in 72% of children.

It should be added, that the level of antibodies showed variations, and even a decrease after 30 and 60 days.

The highest percentage of positive results was obtained for type 3 after 80 days. This percentage comes to the 100% concentration from 1/64 to 1/2048.

In discussing this tabel attention should be called to the fact, that the dosage of the vaccine administered to the children was not the same in all the cases, and at loo ooo $TCID_{50}$,

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has not produced antibodies in 2 children, and the virus failed to develop in their intestines.

In follows from our experiments that the vaccine prepared with the Koprowski strains has fully established its immunogenic properties.

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Table Nr 1

Excretion of CHAT and Fox viruses by individuals viruses

Different doses

The vaccine dose $TCID_{50}$	Number of chil examined	Stool collected I before vaccination	II	III	IV	V after feeding type 3 /Fox/	1V
1 000 000	12	3/12 type 1	11/12	11/12	4/11 type 1		
200 000	11	0/11 type 1	7/11	9/11	3/8 type 1	12/15	1/7 9/16 type 1
100 000	14	0/14 type 1	7/14	9/13	2/13 type 1	1/11 8/11 type 1 type 3	7/11 type 3
T o t a l		3/57	25/37	29/36	9/32	20/26	6/27
		8,1%	67%	80%	28%	76%	59%

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Table Nr 2

The development of antibodies after vaccination with the attenuated Polio vaccine type 1 and type 3

Type	Day of examination	Serum dilution					
		0	4-8	16-32	64-128	256-512	512
1	30	7/33	3/33	14/33	5/33	4/33	0/33
		21%					
1	60	7/24	6/24	4/24	3/24	0/24	4/24
		29%					
1	100	4/25	3/25	3/25	3/25	6/25	6/25
		16%	12%	12%	12%	24%	24%
		16%	12%		24%		48%
3	30	3/24	2/24	3/24	7/24	6/24	3/24
3	80	0/25	0/25	0/25	3/25	6/25	16/25
		0%					
						100%	

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The Spread of Polioviruses in the Population Vaccinated with the Live Attenuated Polioviruses in Comparison with the Nonvaccinated Population

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From the Hygiene and Epidemiological Stations of Liberec and Jihlava,

and from the Virus Department of Institute of Sera and Vaccines, Prague

In connection with the controlled field trial with live poliovirus vaccine in Czechoslovakia in 1958/59

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x) in collaboration with J. Kásová /Olomouc/, V.Potuznik /Budejovice/, D. Rezácová /Praha/, M. Suchánek /Ostrava/, J. Stastna /Usti/, M.Tarabcák /Kosice/ and J.Valihrach (Uherské Hradiste/.

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repeated investigations of the spread of enteroviruses in the vaccinated and nonvaccinated population were made before and after the vaccination of the children with live attenuated polioviruses (Sabin).

This paper presents the results of these investigations made in the period from November 1958 to October 1959.

Material and Methods

In the investigated populations stool specimens were tested for the presence of enteroviruses; the specimens being taken from healthy persons at random, predominantly from children up to the age of 10, partly also from older individuals.

The samplings were done in 4 Czech regions (Liberec, Jihlava, Ústi and Ostrava), in which the children were vaccinated with the three types of attenuated polioviruses and simultaneously also in control regions, in which live poliovaccine had not been used, in the period from December 1958 to February 1959.

In the individual sampling at least 120, but usually even more, of stool specimens were taken in each region, mostly from children institutions (creches, kindergartens,

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nurseries and boarding-schools). From one community only 2 stool specimens were taken maximally, the material was collected in many institutions of the whole region, proportionally to the density of the population.

The time periods in which the individual samplings were made are given in the tables and figures showing the results of the investigations.

The isolation of the viruses was performed from the 10% extract of faeces and 3 tube tissue cultures from monkey kidney cells were inoculated with 0.2 ml of suspension per tube. The isolated cytopathogenic agents were tested against three polio antisera by the current methods used in our Czechoslovac reference laboratory for enteroviruses; the identification of non-polioviruses have not yet been finished.

Results and Conclusions

Figure 1 reviews the results of the investigation of polioviruses spread in all the surveyed regions. The time of sampling is shown in the left lower corner of the figure.

More detailed results of the recovery of entero-viruses from vaccinated and non-vaccinated children in the

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regions in which live vaccine was used, are given in table 1. The analogically arranged results of the spread of viruses in the unvaccinated regions are presented in table 2.

From these tables it is possible to see that before the beginning of vaccination with live poliovirus vaccine no polioviruses were isolated in the region of Liberec, and in the second vaccinated region (Jihlava) two strains of type 1 were recovered.

After feeding a part of the child population with attenuated virus type 1 in December 1958 and type 3 in January 1959, we were able to isolate a great number of type 3 strains in the period of about 14 days after the feeding of type 3 and 1/2 month after feeding the children with type 1, but already in this short period after the mass introduction of the viruses into the population, type 1 virus was isolated in a very small number of children.

In the next sampling carried out already after vaccination with all three types of attenuated polioviruses in the period of approximately two months after feeding with type 2, three months after type 3 and four months after

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feeding the children with type 1, no type 1 strain could be found in a relatively large number of stool specimens tested from the vaccinated population, while viruses of type 2 and 3 occured more frequently, mostly in nonvaccinated children.

After the 1 and 1/2 to 2 and 1/2 months we could not isolate any type 1 strain in the sampling carried out around June 1959; one type 3 strain was recovered from a vaccinated child and only type 2 viruses occured in a greater number in this period.

In the further sampling performed on the peak of the season (September - October 1959), no strains type 1 and 3 were isolated in the vaccinated regions and only two strains type 2 could be found. When calculating the number of isolated type 2 strains to 100 investigated stool specimens we can see that, in comparison with the occurence of polioviruses in the control regions which were not vaccinated, the percentage of isolated type 2 viruses is very low and does not significantly differ from the occurence of type 2 in the population of unvaccinated regions, from which on the other hand we were able to isolate a number of type 1 and 3 strains.

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From the above mentioned results it is possible to suggest that after feeding a part of the child population with type 1 and 3 polioviruses, these viruses did not persist in the vaccinated population for a long time; on the contrary it can be regarded as probable that after a relatively short time these types of polioviruses not only disappeared from the population but could also influence the spreading on naturally occuring type 1 and 3 polioviruses in the vaccinated population.

Only type 2 of attenuated poliovirus administered as the last one seemed to persist in the population for a longer period. The number of isolated type 2 strains is, however, relatively very low and does not significantly exceed the percentage of the incidence of this type of virus in the population of the control regions, in which the children were not vaccinated with the live poliovirus vaccine. It is clear that no mass spread of type 2 poliovirus occured in the vaccinated population, all the more so, as we cannot exclude that both strains isolated in one vaccinated region (Jihlava) are wild, naturally occuring viruses introduced into the population from elsewhere.

On table 3, summarizing the results of investigations

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carried out in the vaccinated and control regions, we can see that on the peak of the season, i.e. in the fifth sampling carried out in September - October 1959 there was a higher incidence of type 1 and 3 polioviruses in the Czech control unvaccinated regions than in the regions where the children were fed. The possible objection that the attenuated polioviruses type 1 and 3 penetrated to the more susceptible population of the neighbouring control regions and persisted there for a longer time, does not seem to be justified. We believe this because:

a) we were not able to prove the spread of individual types of polioviruses in the Czech control regions, which closely communicate with the vaccinated regions, in the investigated samplings up to June 1959, and

b) the greatest part of polioviruses isolated in the control regions in September - October 1959 comes from the region of Gottwaldov, which is neighbouring to Slovak regions of Zilina and Bratislava. As can be seen on table 2 there was a high spread of polioviruses in Slovakia in the summer 1959 and it can therefore be supposed that 5 type 3 and 2 type 2 strains recovered in the fifth sampling in the region of Gottwaldov comes rather from the neighbouring Slovakia than from Czech regions in which the children were vaccinated with live poliovaccine.

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The Spread of Polioviruses in the Vaccinated (with live Polio Vaccine) and Unvaccinated Population of Czechoslovakia

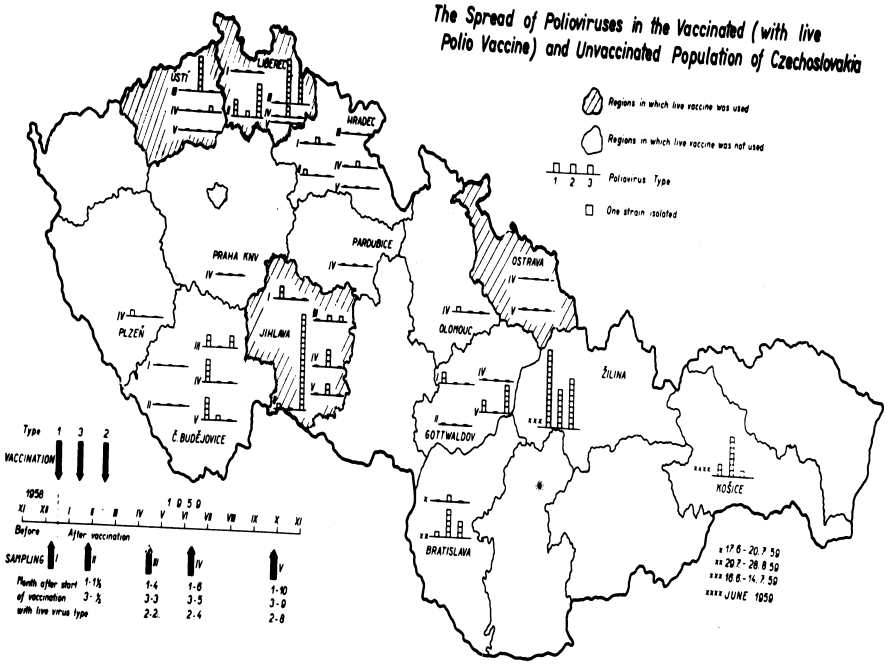

FIG.1

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Table 1

The Occurence of Enteroviruses in the Population of Czech Regions in which Live Poliovirus Vaccine was Used

Vaccinated regions	Live polio vaccine used	Sampling	Data of sampling	Months after start of vaccination	No of stool specimens tested	No of isolated viruses: Polioviruses: Total	Type 1	Type 2	Type 3	Others
Liberec	yes	I	27.XI.-14.XII. 1958.	Before	123	0 +/	0	0	0	1
	yes	I								
		II	23.I.-29.I.59	1 1/2	130	9/1	3/0	0/1	6/0	2/0
		III	10.IV-22.IV.	4	242	6/7	0	3/5	3/2	0/2
		IV	25.V-10.VI	5 1/2	193	0/2	0	0/2	0	0/1
		V	24.IX-5/X	9 1/2	150	0	0	0	0	0/2
Jihlava	yes	I	2.-11.XII 58	Before	119	2	2	0	0	5
		II	23.-31.I. 1959	1 1/2	115	11/7	0/1	0	11/6	0
		III	11.-20.IV	4	121	1/7	0	1/0	0/1	0
		IV	21.V.-9.VI	5 1/2	149	1/2	0	1/2	0	1/0
		V	30.IX.-10.X	9 1/2	188	0/2	0	0/2	0	4/11
Usti n/L.	yes	I			Not done					
		II			Not done					
		III	9.IV.-4.V.59	4	193	6/2	0	4/2	2/0	1/1
		IV	25.V.-5.VI	5 1/2	213	1/0	0	0	1/0	0/4
		V	1.-8/X.	9 1/2	111	0	0	0	0	0
Ostrava	yes	I			Not done					
		II			Not done					
		III			Not done					
		IV	24.VI.-7.VII	6 1/2	131	0	0	0	0	0
		V	12.-22.X	10	142	0	0	0	0	0/5

+/ Nominator: of isolated strains of viruses from the vaccinated persons.
Denominator: of isolated strains of viruses from the unvaccinated persons.

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Table 2

Spread of Enteroviruses in the Population of Czechoslovak Regions in which Live Poliovirus Vaccine Was Not Used

Region	Sampling	Date of sampling	N° of stool specimens tested	N° of isolated viruses				
				Polioviruses				
				Total	Type 1	Type 2	Type 3	Others
Hradec	I	5.-15.XII. 1958	III	1	0	1	0	3
	II	10.-11.II. 1959	93	1	1	0	0	0
	III	22.29.IV.	90	0	0	0	0	4
	IV	3.-5.VI.	174	1	0	1	0	6
	V	1.-20.X.	130	0	0	0	0	0
C.Budejovice	I	December 1958	91	0	0	0	0	1
	II	February 1959	30	0	0	0	0	0
	III	April	161	4	2	0	2	5
	IV	3.-26.VI.	219	4	4	0	0	2
	V	10.X.-20.XI	180	5	4	1	0	11
Gottwaldov	I	December 1958	91	2	2	0	0	4
	II	10.-21.11. 1959	120	0	0	0	0	0
	III					Not done		
	IV	25.V.-11.VI	230	0	0	0	0	5
	V	22.IX.-30/IX	129	7	2	0	5	2
Pardubice	I-III					Not done		
	IV	12.-22.VI. 1959	118	0	0	0	0	5
Praha KNV	I-III					Not done		
	IV	22.-29.VI 1959	127	0	0	0	0	2
Plzen	I-III					Not done		
	IV	2.VI.1959	112	1	1	0	0	3
Olomouc	I-III					Not done		
	IV	16.VI.1959	115	1	1	0	0	9
Bratislava (Slovakia)	x)	17.VI.-20/VII 1959	173	1	0	1	0	22
	xx)	29.VII-28/VIII	154	9	1	5	3	32
Zilin (Slovakia)	xxx)	16.VI.-14.VII. 1959	206	31+)	14	7	9	9
Kosice (Slovakia)	xxxx)	June 1959	101	10	2	7	1	3

+) mixture of polio and other virus.

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Table 3

The Spread of Enteroviruses in the Vaccinated (with Live Polioviruses/ and Unvaccinated Population of Czech Regions

Region	Live polio vaccine used	Sampling	Months after start of vaccination	Stool specimens tested No.	From vacc. / unvacc. persons	Polio type 1 No.	Polio type 1 per cent	Polio type 2 No.	Polio type 2 Per cent	Polio type 3 No.	Polio type 3 Per cent	Others No.	Others Per cent
Liberec Jihlava	yes	I	Before	242		2	0.8	0	0	0	0	6	2.5
Liberec	yes	II	1 1/2	245	47	3	6.58	1	0.05	17	36.17	2	0.82
Jihlava					198	1	0.5	1	0.5	6	3.03	0	0
Liberec	yes	III	4	556	106	0	0	8	7.5	5	4.7	1	0.9
Jihlava Ústí m/L.					450			7	1.6	3	0.3	3	0.7
Liberec	yes	IV	5 1/2	686	140	0	0	1	0.7	1	0.7	1	0.7
Juhlava					546	0	0	4	0.7	0	0	9	1.6
Ústí n/L. Ostrava													
Liberec	yes	V	9 1/2	591	140	0	0	0	0	0	0	4	2.8
Jihlava					451	0	0	2	0.4	0	0	18	4.0
Ústí n/L. Ostrava													
Hradec C.Budejovice Gottwaldov	not	I		293		2	0.7	1	0.3	0	0	8	2.7
Hradec Gottwaldov C.Budejovice	not	II		243		1	0.4	0	0	0	0	0	0
Hradec C.Budejovice	not	III		251		2	0.8	0	0	2	0.8	9	3.6
Hradec C.Budejovice Gottwaldov Pardubice Praha KNV Plzen Olomouc	not	IV		1095		6	0.5	1	0.1	0	0	32	2.9
Hradec C.Budejovice Gottwaldov	not	V		439		6	1.4	1	0.2	5	1.1	13	3.0

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STAT

Experimental tests of candied live poliovirus vaccine in tissue culture

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In April-July 1959 on Professor M.P. Chumakov's initiative 1 experiments were made for elucidating the possibility of including live poliovirus vaccine into candy mass (Bezzubov, A.D., Fleer, G.P., Chumakov, M.P., 2). Examination of the vaccine titers in mixtures with sugar and candy mass showed good preservation of the virus at certain temperatures (Fleer, G.P., 2). Satisfactory results were obtained in investigations of the establishment and immunogenic activity of candy-vaccine in the vaccinated children (Fleer, G.P., 3 , Voroshilova, M.K., Taranova, G.P. 4).

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In September 1959 the Institute for Poliomyelitis Research of the Academy of Medical Sciences, USSR, together with All-Union Scientific Research Institute of Candy Industry (Professor A.D. Bezzubov) developed Technical Requirements for production of live poliovirus vaccine in the form of dragée-candy.

After these Technical Requirements had been approved by State Sanitary Inspection of the USSR and Technical Department of Moscow City Council of national economy Marat Candy factory started large-scale production of dragée-candies containing mono- or trivalent live poliovirus vaccine.

Each lot of the candied poliovirus vaccine was virologically tested at the Department of biologic control of viral preparations of the Institute for Poliomyelitis Research, AMS, USSR. For the manufacture of dragée live poliovirus vaccine was used from Sabin attenuated poliovirus straines type I - LSc, 2 ab; type II - p 712, CH, 2 ab and type III - Leon, 12a,b, which had passed through all the stages of animal and tissue culture control tests 6 .

In the process of dragée manufacture the vaccine is thoroughly mixed with syrup cooled to 25^{0}C (pH 6.8-7.2) containing 69% sucrose, 8% glucose, 8% fructose, 15% water

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and small amount of food dye. During 1-1.5 hours in roller boiler at a temperature up to +25°C a strictly definite by volume quantity of syrup with the vaccine is evenly distributed, with addition of sugar powder, into approximately 30,000 crystal sugar granules. Then in the same boiler outer sugar-fatty-waxy cover is deposited on the resulting spherical dragée-candies for prevention of their drying up.

The amount of live poliovirus vaccine introduced into candy mass varied in different vaccine lots from 50,000 to 350,000 TCD of virus per one dragée-candy weighing 1 gm, and on the average was about 100,000 TCD.

The technology of dragée manufacture in roller boilers allows ± 15% variations in the weight of individual candies which is of no great significance for vaccine dosage because of considerable excess of the amount of cultural units of the vaccine virus introduced into candies (according to experimental data of a number of investigators, a minimal immunizing dose of the live vaccine is about 10,000 TCD of poliovirus).

The whole process of manufacture of dragée-candy with the vaccine (including packing in parcels) goes on at room temperature not higher than 25°C and is over in 3-4 hours.

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The finished dragée with the vaccine is stored until shipment to consumers at -20° C. During transportation of dragée-vaccine (mainly by air) and until use for immunization it is allowed to keep the kandy at room temperature not longer than for 3-7 days, and at +4° C not longer than 1 month.

The present paper describes the results of titrations of the candied live poliovirus vaccine and the results of tests for virus preservation in candy at different temperatures and after different periods of storage.

Methods.- The candied poliovirus vaccine was titrated by the plague method [7] modified by Hsiung and Melnick [8].

Dragée-candies (average weight of 1 piece - 1 gm) were dissolved in medium 199, containing penicillin and streptamycin, 1000 units per ml, each. Dilutions of dragée from 1 = 200 to 1:750 were prepared in this medium. 0.1 to 0.2 ml of each dilution was added in each of 2-3 bottles with 7-day culture of trypsimized rhesus monkey kidney cells (the surface of cell monolayer = 60 cm^2). Inoculated cultures were kept for 1 hour at + 37° C, layered with agar and then again incubated at +37° C. The results were read at 5 days.

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Results

In the first stage of the work titrations were made with experimental samples of candied vaccine manufactured in small amounts. The findings indicated that from 70.9 to 94.3% PFU of live poliovirus vaccine was preserved in the process of dragée manufacture which confirmed the acceptability of technology for candied vaccine manufacture at Marat factory.

Subsequently in process of production manufacturing of the candied vaccine at the factory loss of the virus was found to be negligible.

According to technical conditions for manufacture of the live poliovirus vaccine in the form of dragée-candy each candy is allowed to contain 100,000 $\pm$ 50% of virus particles. In connection with this for production manufacturing of the candied vaccine such doses of the live vaccine were selected which provided for sufficient content of virus particles in dragée-candies. This is shown by the results of titrations done for control of production lots of the candied vaccine presented in Table 1.

It may be seen from the data in Table 1 that when a liquid monovaccine was used one dragée-candy contained at

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least 70,000 (7×10^4) plague-forming units, and with trivaccine one dragée contained over 227,000 (2.27×10^5) PFU.

In the process of manufacturing large lots of the candied vaccine not less than 83.8% PFU was preserved, as a rule, in one dragée-candy.

Table 2 presents the results of investigations on eveness of distribution of virus particles in dragée from one batch of the candied vaccine. For this experiment dragée were taken from different boxes with the finished vaccine.

The data in Table 2 show that the virus distribution to individual dragée is sufficiently even. (The ratio showing variation of the virus content in dragée is 17.4%, and the doubled error of arithmetic mean is $\pm$ 16,200).

Tables 3 and 4 present results of titrations of the candied live vaccine after various periods of storage at different temperatures.

These data indicate that the storage of the candied vaccine at sub-zero (-20° C) and refrigerator ($+4^{\circ}$ C) temperatures does not cause any significant losses of virus particles in dragée.

When the candied live vaccine is stored at room temperature for 10 days or longer the number of plague-forming units in dragée is reduced by 50 per cent or more.

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Conclusions

1. The technology of manufacture of the candied live poliovirus vaccine makes it possible to produce candies with any amount of virus particles necessary for immunization, in one dragée.

2. The candied live poliovirus vaccine stands storage at +4°C and - 20°C.

3. Storage of the candied poliovirus vaccine at room temperature for periods longer than 10 days causes significant loss of the virus in dragée. The decline in titer begins already 3-5 days after storage at room temperature. Therefore it is recommended to store the dragée-vaccine at room temperature for periods not longer than 3-5 days.

References

1. Chumakov, M.P., Voroshilova, M.K., Drozdov, S.G., Dzagurov, S.G. and others - "On mass oral immunization of population in the Soviet Union against poliomyelitis with live vaccine from A.B. Sabin's attenuated strains", published by the Institute for Poliomyelitis Research, AMS, USSR, pp.1-77, Moscow, 1960.

2. Bezzubov, A.D., Fleer, G.P., Chumakov, M.P. - Experimental data on the possibility of including live polio-

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

virus vaccine into candy. Proceedings of the IV-th Conference of the Institute for Poliomyelitis Research, AMS, USSR, May 17-20, 1960. Manuscript.

3. Fleer, G.P. Virologic and serologic evidence of immunization of children with candy containing live poliovirus vaccine.- Ibid, May 17-20, 1960.

4. Voroshilova, M.K., Taranova, G.P.- Unpublished data.

5. Sabin, A.B.- F J.Am.Med. Assn. 1956, 162:1581,

Ibid, 1957, 164:1216.

Brit.Med. J. 1959, 1:663.

6. Chumakov, M.P. and others.- Problems of Virology,1959:529.

7. Dulbecco, R. & Vogt, M.- Ann. N.Y. Acad. Sci.,1955,61:791

8. Hsiung, G.D. & Melnick J. - J.Immunol.1957,78:128; 1958, 80:282

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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Table 1

Results of control titrations of production lots of the candied live poliovirus vaccine

Date of dragée manufacture	Date of titration	t° and period of storage	number of PFU in vaccine given per 1000 dragée candies (1 kg)	Estimated number of PFU per 1 dragée by titration	Number of PFU per 1 dragée by titration	Ratio of actual to estimated number of PFU per 1 dragée	Virus type and lot number
12.I.1960	6.I. 1960	-20°C 3 days	89.13×10^6	89×10^3	88.75×10^3	99.5%	I; N.25
15.I.1960	16.I. 1960	-20°C 1 day	241.85×10^6	242×10^3	227.188×10^3	93.9%	I, II, III, Nos. 25, 31, 28
1.II.1960	5.II. 1960	-20°C 3 days	12.5×10^6	125×10^3	120.625×10^3	96.5%	III; No. 34
3.II.1960	5.II. 1960	-20°C 1 day	250×10^6	250×10^3	$216,563 \times 10^3$	86.6%	III; No. 34
4.II.1960	5.II. 1960	-20°C 12 hrs.	60.26×10^6	60×10^3	70×10^3	116%	I; No. 23
10.II. 1960	11.II 1960	-20°C 12 hrs.	79.62×10^6	79×10^3	79.375×10^3	99.7%	I; No. 35
17.II. 1960	16.III 1960	-20°C 26 days	$141,58 \times 10^6$	142×10^3	124.375×10^3	87.7%	III; No. 34
25.II. 1960	9.III 1960	- 20°C 12 days	87.1×10^6	87×10^3	83.75×10^3	93.8%	I; No. 25
29.II. 1960	25.III 1960	- 20° C	174.2×10^6	174×10^3	170.625×10^3	90.8%	I; No. 25

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Table 2

Distribution of virus particles in the candied live poliovirus vaccine

Virus type in dragée	Vaccine lot number	Number of PFU in vaccine given per 1000 dragée candies	Dragée number	Number of plagues in bottles			Number of PFU in 1 dragée candy	Average number of PFU in 1 dragée candy (M)	Mean square deviation (σ)	Doubled error of arithmetic mean (2xSD)	Variation ratio (V)
				Bottle 1	Bottle 2	Bottle 3					
			1	124	131	121	125×10^3				
			2	144	124	160	143×10^3				
			3	134	174	148	152×10^3				
			4	180	187	194	187×10^3				
I, II, III	Trivaccine No. 21	162.69×10^6	5	178	138	164	160×10^3				
			6	160	137	194	130×10^3	147×10^3	25.6×10^3	$\pm 16.2 \cdot 10^3$	17.4%
		Estimated number of PFU in 1 dragée candy = 162×10^3	7	209	148	194	184×10^3				
			8	133	163	179	158×10^3				
			9	128	130	115	124×10^3				
			10	113	109	110	111×10^3				

Notes:

1) 0.1 ml of $10^{-2.0}$ dilution of dragée was added to each bottle

2) σ - mean square deviation

M - average number of PFU in 1 dragée-candy

V - variation ratio $\frac{\sigma}{M} \times 100\ \%$

3) 2·SD = doubled error of arithmetic mean

4) $SD = \frac{\sigma}{\sqrt{n}}$; n - number of observations .

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Table 3

Preservation of the virus in the candied live poliovirus vaccine at different temperatures

Virus type in dragée	Conditions of storage	Period of storage (days)	Number of PFU in 1 dragée-candy	Ratio of number of PFU to control %
I	+18°+22°C (in the room)	3	72.5×10^3	96.6%
		5	44.375×10^3	59.2%
Lot No. 25	+ 4°C (in refrigerator)	3	78.125×10^3	104.1%
		5	65×10^3	86.6%
	-20°C (control)	10	75×10^3	100 %
	+18°+22°C (in the room)	10	34.375×10^3	19.8%
I	+4°C (in refrigerator)	10	161.25×10^3	92.6%
Lot No. 25	-20°C (control)	15	173.125×10^3	100 %
I	+18°+22°C (in the room)	15	33.125×10^3	20.2%
Lot No. 23	+4°C (in refrigerator)	15	96.825×10^3	83.7%
	-20°C (control)	30	114.375×10^3	100 %
	+18°+22°C (in the room)	15	13.125×10^3	18.7%
II Lot No. 31	+4°C (in refrigerator)	15	73.125×10^3	100.4%
	-20°C (control)	30	70×10^3	100 %
III Lot No.34	+18+22°C (in the room)	15	47.5×10^3	37.2 %
	+4°C (in refrigerator)	15	136.875×10^3	107.3 %
	- 20°C (control)	30	127.5×10^3	100 %

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Table 4

Preservation of the virus in the candied live poliovirus vaccine at subzero temperature (-20° C)

(Experimental lots)

Date of dragée manufacture	Virus type	Date of titration	Period of storage (days)	Number of PFU in the vaccine given per 1000 dragée-candies (1 kg.)	Estimated number of PFU in 1 dragée-candy	Number of PFU in 1 dragée candy by titration
3.XI.59	III	9.III.1960	125	53.4×10^6	53.4×10^3	60×10^3
4.XI.59	III	9.III.1690	124	53.4×10^6	53.4×10^3	52.5×10^3
18.XI.59	II	18.III.1960	91	37.77×10^6	37.77×10^3	31.9×10^3

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SOME RESULTS ILLUSTRATING THE WORK ON MASS IMMUNIZATION OF THE POPULATION IN THE SOVIET UNION WITH LIVE POLIOVIRUS VACCINE PREPARED FROM THE STRAINS OF ALBERT B. SABIN.

Chumakov,M.P, Voroshilova,M.K.,Drozdov,S.G., Dzagurov,S.G., Dobrova,I.N., Ashmarina,E.E., Shirman,G.A., Fleer,G.P., Tolskaya,E.A., Yankevich,O.D.,(Moscow).

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Principal results of the work on mass immunization of the population in the Soviet Union with live poliovirus vaccine prepared from A.B.Sabin's strains and carried out under the guidance of workers of the AMS USSR Institute for poliomyelitis research were contained in a specially issued Report No.2,published in russian and english (77 pages including supplements, publication of the Institute for poliomyelitis Research,Moscow,1960).

These results were subject of detailed discussions on two occasions and found approval of the Presidium of the Academy of Medical Sciences of the USSR, a supreme scientific centre of medical research in the USSR, authorized of approving new proposals in the field of prevention and treatment of diseases. On the basis of a recommendation made by the Presidium of the AMS of the USSR and of a resolution passed by the Board of the Ministry of Public Health of the USSR, an order dated 16.XII, 1959 was issued by the Minister of public health of the USSR providing for mass immunization with live poliovirus vaccine during 1960, and mainly up to July 1960,of the population in the age=group from 2 months up to 20 years, this comprising, approximately 35% of the entire population of the country, or around 77 million persons.

It is an impressive task that has been set for the first time in our country and, for that matter, in the world at large, to vaccinate in the space of just one year many millions and thus eliminate epidemic manifestations of poliomyelitis on a scale of a large country. A successful solution of this task will in a large measure influence further developments of specific poliomyelitis prophylaxis in our and other countries.

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To day we can make a short communication on certain preliminary results following realization in 1959-1960 of a broad program of immunization with live poliovrius vaccine, covering that part of it,which involves efforts of the AMS USSR institute for poliomyelitis research.

But, first of all, I should like to point out here a particularly outstanding part played by Professor Albert B. Sabin in raising and realizing the task involving mass immunization of the population with live poliovirus vaccine. His was the merit of succesefully accomplished selection of three poliovirus vaccinal strain types and their detailed evaluation. He has supplied us with the high=quality initial culture material for the preparation in our country of live vaccine in amounts necessary for large=scale immunization. On many occasions he rendered great services to us by sharing his vast knowledge in the domain of poliomyelitis and has been very active in organizing fruitful international collaboration among virologists in matters concerning the study and wide use of live poliovirus vaccine. For all this I should like to say to Professor Albert Sabin our heartiest russian-thanks! We shall never forget that valuable contribution which Albert B.Sabin has made to the theory and practice of poliomyelitis control in our country.

Poliomyelitis is a grave, but relatively rare affection. And,nevertheless,it proved necessary to introduce extremely broad measures to create artificial immunity in the entire population of the country by means of mass vaccination within very narrow time=limits in order to combat this uncommon disease.

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The explanation of this should be sought in the fundamental features peculiar to poliomyelitis as an infection having a great number of completely symptom=free forms, hard to diagnose. Therefore, it is only with the aid of broadest measures designed to rapidly produce artificial immunity in the whole of the susceptible population that the menace of poliomyelitis epidemics can be averted.

To achieve this, an effective, fully accessible and completely harmless vaccine, free of any reaction, is needed, which would not call forth any difficulties during its large= scale application.

Trial tests of live poliovirus vaccine, carried out in a number of countries and, particularly, in our country during 1959, furnished a convincing proof that it is just the live vaccine that is most suitable as a preparation for mass immunization.

As contrasted to the killed Salk vaccine great advantage of the live one lies in its ability to produce in the organism of the vaccinated a more or less complete resistance of the tissue cells to infection at the "portal of entry". This phenomenon will, apparently, make it possible to steeply reduce the circulation among the population of wild epidemic strains of ~~the~~ poliovirus, this being accomplished as a result of a series of repeated vaccinations with attenuated viruses. Thus an important pre=requisite is being created, which will enable to do away with the epidemics of poliomyelitis.

One of the objections which is most often raised against the use of live poliovirus vaccine is the apprehension of a possible reversion (restoration) of pathogenic properties in attenuated strains of the poliovirus occurring under the effect of

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selection of individual virulent viruses ,taking place in th intestine of humans, and repeated passages thereof among susceptible subjects.

There are many facts available at present testifying to a sufficient stability of genetic signs in attenuated strai of A.B.Sabin, which persists within the limit of several p sages via the human body. However, there are no theoretic and experimental grounds which would make it possible to tirely exclude the possibility of degeneration occurring the vaccinal strains under the effect of their being cult. in inappropriate conditions, or due to a long=term select of virulent species of the virus and their multiplication the course of passages thrgugh susceptible humans. We know that under certain conditions it is possible to single out from a vaccinal strain forms with elevated virulence, as c pared to that existing in the initial population of the va cinal virus. The crux of the question is only how long and how many passages via the cultures or through the human bc it will take to restore the neuro pathogenecity of the vac virus. The numerous data now available prove that the reve process or the pathogenicity restoration in properly puri vaccinal strains are considerably longer and unstable pro cesses than that underlying the development of immunity i the population following introduction of vaccinal strains.

In connection with this we put forward in 1958-1959 principle of a mass and synchronous character of peroral i nization with live poliovirus vaccine, covering the territor of a whole district, city or region, so as to ensure maxi immunization coverage in the shortest possible time and to duce to the minimum the possibility of a lengthy circulat

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of any policvirus strains among susceptible subjects and of its rising neurovirulence during serial passages in children.

What is actually needed is that the process of the rapidly extending immunization counteracted effectively the reversion process, thus eliminating conditions favorable for repeated passages. In carrying out mass vaccinations during 1959-1960 we closely adhered to this principle.

Mass immunization of the population with live vaccine prepared from A.B.Sabin's strains was being effected in 1959 in 14 republics of the Soviet Union on an ever increasing scale.

At the end of the year the total number of vaccinated throughout the country exceeded 15 200 000 persons (see table 1). Of these about 1 670 000 subjects were immunized under surveyance of Prof. Smorodintsev and his collaborators with the vaccine prepared in Leningrad, and over 13 500 000 persons- under supervision of our institute, with the vaccine produced in Moscow. The global number of the population residing in districts covered by the vaccinations in 1959 comprises around 65 millions, or approximately 1/3 of the entire popuation of the country. Over 2 500 000 persons received live vaccine in 1959 in the shape of liqueur=bonbons / in the Azerbeidjan, Armenian, Georgina,SSR, in the Khabarovsk territory and, partly, also in the Moscow region/. The remaining immunized persons were given two drops each of liquid vaccine, diluted in proportion 1:10, measured out with an eye pipette.

The use of live vaccine in the shape of liqueur=bonbons proved to be a further step in the direction of mass immunization against poliomyelitis. In consideration of the unusually large scope and narrow time limits set for peroral immunization

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it would be extremely difficult to secure the dilution of defrosted liquid vaccine and its distribution dropwise throughout the country by the local medical staff in the field.

In this conjunction, the Institute for poliomyelitis research in cooperation with the research institute of confectionary industry has elaborated a new presentation of live vaccine inside pasty candies and, later on, in the shape of liqueur=bonbons. This was based on the data proving satisfactory preservation of vaccinal strains in strong solutions of inactive sugars and in the sweetmeat mass at negative temperatures- for a space of no less than 3 months, at +4°C - for about a month, and at room temperature - for 3-5 days. The tests for the adaptability and immunogenecity of live vaccine presented in the shape of liqueur=bonbons, as effected in 1959 by G.P.Fleer in the city of Klin, in Moscow region, showed quite satisfactory results , which could be favorably compared with those obtained in immunization with liquid live vaccine / see tables 2,3 and the diagram 4/.

In autumn of 1959 workers of another laboratory (Voroshilova, M.K., Terenova, G.P., and others) again verified the immunogenecity of live vaccine in the liqueur=bonbons presentation, and also obtained good results / they found rising number of antibodies in the vaccine of the I and 3 types, presented in the shape of liqueur=bonbons used for immunization after their storage at room temperature for three days-see table 4/.

The immunization technique itself, involving presentation of the vaccine in candies, turned out to be extremely convenient and attractive in every respect.

All this contributed to a wider employment of liqueur= bonbons with live vaccine for the purpose of policvirus immu-

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nization. Production of liqueur=bonbons with vaccine in the amount of up to 3 tons a day was set up at the confectionary factory "Marat".

In 1960 the vast majority of poliovirus inoculations (around 90%) were effected with live vaccine in the shape of liqueur=bonbons and only 10% - with liquid vaccine, dispensed dropwise, this latter, chiefly, for immunization of nurslings, unable to suck candies.

There are several reports presented at this conference that characterize the ability of live vaccine to preserve its properties in liqueur=bonbons at different thermal regimes, the standard nature of vaccinal doses with variable amounts of the vaccinal virus in different kinds of bonbons, and also virological and serological data relative to the examination of those immunized with the confectioned vaccine.

According to the order issued by the Ministre of public health of the USSR on mass poliovirus vaccinations in 1960 the Institute for poliomyelitis research was charged with the task of supplying live vaccine and exercising methodical guidance over vaccinations throughout the whole country. In conformity with this, the institute has elaborated and the Ministry approved methodical directions for organization of immunization with live vaccine and also instructions for the use of liqueur=bonbons with live vaccine in peroral immunization against poliomyelitis.

The preliminary results showing fulfillment during 1960 of the program for mass immunization of the USSR population aged up to 20 years are as follows:

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A total of 145 980 000 inoculating doses of live vaccine prepared in Moscow from the A.B.Sabin's strains were distributed throught the country during the first four incomplete months of 1960 / data as of 21.IV,1960/. This included monovaccine of the I type- 67 580 000 doses, of the 3 type - 41 026 000 doses, of the 2 type - 17 351 000 doses and 20 023 000 doses of a trivalent mixture / 1,2,3 types/used in revaccination of those who had been immunized previously with individual types of live vaccine / 3 543 000 doses of the trivalent vaccine was distributed for the primary vaccination/.As of 21.IV.1960 altogether 71 123 000 inoculating doses were distributed for primary vaccination (I type or a trivalent mixture)

Table 5.

DISTRIBUTION OF LIVE POLIOVIRUS VACCINE FROM THE A.B.SABIN'S STRAINS ACCORDING TO INDIVIDUAL REPUBLICS OF THE USSR FROM THE I.I.1960 TILL 21.IV.1960.

Republics	The number of distributed inoculating doses in thousands					
	Monovaccines			Trivalent mixture of I, 2,3 type	Total	Including that used for primary immunization
	I type	2 type	3 type			
Russian Federation	36.336	10.637	29.047	2.202	80.222	32.336
Ukraine . . .	12.080	3.512	7.713	6.140	29.445	12.887
Bielorussia	3.000	3.000	2.976	-	8.976	3.000
Uzbekistan . .	3.176	200	200	4.406	7.922	3.500
Kazakhstan . .	2.294	-	120	3.022	5.436	3.600
Georgia . . .	1.500	-	-	-	1.500	1.500
Azerbaidjan . .	1.404	30	-	-	1.434	1.400
Moldavia . . .	600	-	-	900	1.500	1.100
Lithuania ...	750	-	-	-	750	750
Latvia	530	70	70	400	1.070	700
Kirhgizia . . .	800	-	-	998	1.798	800
Tadjikistan . .	750	-	-	1.101	1.851	750
Armenia/in XII.59-900.000/	-	902	900	-	1.802	900
Estonia	282	-	-	874	1.156	800
Turkmenistan . .	1.478	-	-	-	1.478	1.100
TOTAL	67.580	17.351	41.026	20.023	145.980	71.123

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Since a great deal of work connected with immunization of the population with live poliovirus vaccine was already done in many republics during 1959 (Estonian, Lithuanian, Georgian, Azerbaidjan, Moldavian, Uzbek, Tadjik, Kirhgiz, Turkmen SSR) there will be carried out in these areas only 2 inoculations in 1960:- the first with the I type of monovaccine and the seoond- with the trivalent mixture / 1.2 and 3 types/of live vaccine, which will cover the entire population aged from 2 months to 20 years.

In the Russian Socialist Federation, Ukrainian SSR, Latvia and Armenia immunization is threefold with monovaccines. In some regions of the Ukraine it is effected twice with a tri-- valent mixture, while in the other regions of this republic- separately with monovaccines.

There are no precise figures available at present showing the factual numbers of immunized with live vaccine in 1960. But taking account of the usual losses incident to the distribution of vaccine during inoculations (around 15-20%) one may approximately set the figure of those vaccinated in the USSR during the first quarter of 1960 at about 55 million (about 70% of the population aged up to 20 years). All of these have already received the I type of live poliovirous vaccine, while 15.000.000 among them have received in 1960 also the III type of monovaccine and about 4 millions have completed all the three vaccinations. Over 14 millions immunized with live vaccine in 1959 have been revaccinated in accordance with the programme of 1960. Vaccinations were under way also in April and May 1960.

In addition to the amounts of the preparation necessary to ensure the fulfillment of internal program of mass immuniza-

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tion with live poliovirus vaccine from Sabin's strains, the Soviet Union passed on by way of friendly assistance vaccines of the 1,2 and 3 types separately for 2.5 million children; to Hungary; vaccines of the 3 and 2 type for 1.5-2.0 millions - to Czechoslovakia; for 1.5 millions - to the people's republic of Viet=Nam; for 2.2 million children- to Bulgaria. Albania and China also received some of it (small amounts).

We have no doubts that the big program envisaged by us for immunization with live vaccine in 1960 will be fulfilled. It goes without saying that such a scope and pace of immunization against poliomyelitis would have been quite impossible with killed Salk vaccine. It is only peroral immunization with live poliovirus vaccine presented in the shape of liqueur=bonbons that makes it possible to accomplish mass vaccination of susceptible population within short periods of time. And this garantees radical prevention of poliomyelitis epidemics.

Poliovirus vaccinations were being effected by the district medical field establishments on strictly voluntary bases, with maximal assistance on the part of the population, this being due to a broadly organized sanitary propaganda (through the press, radio, TV, motion=pictures, lectures,individual talks, leaflets,etc.).

In 1959, in the areas covered by vaccinations there were set up advisary teams comprising experienced physicians, charged with detailed investigation of all cases involving the central nervous system and suspicious of poliomyelitis. Epidemic groups were created in the Estonian and Lithuanian SSR for detection and investigation of all poliomyelitis cases. In addition to this, special travelling groups were organized in Estonia , Lithuania, Moscow region, Karaganda, in in Sverdlovsk, Oren-

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burg and other regions. Over 2.000 persons underwent serological and virological examinations in the areas covered by immunization. The practice of laboratory diagnosis in the areas of vaccinations was considerably broadened and substantiated in the baltic republics, in Tashkent, Alma=Ata, Karaganda, Mosoow and other regions. This enabled us to considerably improve the organization of mass vaccinations and to set up and maintain a thorough observation of the vaccinated, as well, to broaden diagnostic findings with regard to poliomyelitis, and to secure adequate and complete recording of all polio=cases at the time of and after vaccinations. At many vaccination posts in establishments for children, long=term control observations were being conducted over the temperature and general condition of vaccinated and contact children.

Basing upon the research work and trial tests in the field effected by our institute conjointly with other scientific bodies there can be drawn several conclusions with regard to the major problems involving the study of live poliovirus vaccine:

1. Innocuousness of live vaccine. It can be taken for granted now that the live vaccine obtained from the A.B. Sabin's strains is a completely harmless preparation, free from any untoward reactions,-provided its production is effected under observation of certain conditions. Large=scale field tests of the vaccine have only confirmed this fact. The tests for the verification of the live vaccine safety during its production, possibly, still require some degree of simplification and improvement, but even so as they are, they ensure reproducible character of the end=results.

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Under conditions of a synchronous mass immunization of the entire susceptible population in a region the problem of reversion of pathogenic properties in the live poliovirus vaccine proved practically non-existant. There were no poliomyelitis cases on records in the Soviet Union that could be attributed to the immunization with live vaccine from the Sabin's strains.

Untoward reactions incident to poliovirus vaccine were studied by many physicians on the basis of registered complaints put forward by the vaccinated. Specialists hold that under conditions prevailing during mass immunization there may be instances when vaccinations coincide with all kinds of symptoms produced by other affections. It was impossible to establish any relationship between various complains and symptoms and the effect of the vaccine. The total number of the, so-called, reactions to the vaccine itself is very insignificant (no more than 3 per 100 000). The question relative to the untoward reaction to live vaccine, apparently, requires some further and more detailed study, but is now of no great practical importance.

2. Immunological activity of live poliovirus vaccine.

Workers of our institute, as well as the laboratories in Tashkent, Riga and some other places have carried out very extensive serological investigations based on the materials of several thousands twin blood tests in those immunised with live vaccine under different epidemiological conditions, or in connection with the employment of varying vaccination schemes.

As a rule, these investigations demonstrated the advantages of live vaccine, both with respect to the speed with which immunization sets in and its actual duration.

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The most frequently used immunization scheme in the Soviet Union during 1960 has been that with individual monovaccines / I -3 -2 types/ with subsequent revaccination with a trivalent mixture. As will be stated later at this conference the experience of 1959 demonstrated the scheme 1 - 3 -2 to have yielded optimal serological results. Along with this, schemes providing for single or twofold vaccination with a trivalent mixture have been subject to large=scale tests in 1959 and 1960, which, judging by serological data and epidemiological observations of 1959 have also ended with fairly good results. It would, evidently, be more advisable to have a choice of several immunization schemes with live vaccine, depending upon relevant epidemic indications and local conditions. The results of serological investigations point to the influnce exercised by the time=factor upon gradual rising of immunological response in the inoculated subjects to vaccination, viz; the results of examinations for antibodies 3 months after immunization with the I type were definetly better than 1 month thereafter.

In the course of observations on the isolation of the vaccinal viruse from the feces during revaccination it could be established that, as distinct from the killed Salk's vaccine, the live poliovaccine produces not only humoral, but, in a certain measure, also local immunity, i.e. immunological resistanse of cells in the gastrointestinal tract. This may result in a progressive restriction of poliovirus strains circulation among the population.

The problems associated with the dynamics in the development of local immunological resistance to policvirus demand, however, some further study and more precise definition.

3. The Virus=carrier State and contact transmission.

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As evidenced by numerous observations, including those performed in our institute, peroral immunization with live poliovaccine is accompanied by a more or less protracted excretion of vaccinal strains together with the feces. The duration of the virus excretion in children without antibodies is, approximately, twice as long as in those possessing them. All those susceptible to poliomyelitis, who contact vaccinated subjects, within a very short space of time receive vaccinal viruses and become immunized latently. No untoward facts could be noted in connection with the virus-carrier state and transmission of vaccinal viruses. Quite the contrary, it is firmly established that the virus-carrier state and contact transmission during mass immunization with live vaccine represent an exceptionally favorable factor, conducive to an all-round and more rapid immunization within families and collective bodies.

4. Interference. In peroral immunization with live poliovirus vaccine especial importance acquire the phenomena of interference between the street and vaccinal poliovirus strains, between non-poliomyelitic enteroviruses (ECHO and Coxsaki groups) and live vaccine, and also interference among individual types of live vaccine inside the groups themselves.

As a result of extensive investigations it has been found that interference between the vaccinal and other enteroviruses occurs under various epidemiological conditions with varying frequency and in different months of the year. Winter months are, apparently, most advantegious for the vaccination. The data on hand enable us to draw a preliminary inference to the effect that most instances of failure in peroral immunization are due to the influence exercised by interference on the vaccinal process.

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The interference may, probably, be overcome by resorting to a particularly massive vaccination / with no less than 50% of the susceptible population covered by inoculations/ and as a result of repeated vaccinations over a period of 1-2 years..

The necessity should be stressed of a further, more complete study of regularities governing the interference between enteroviruses ~~and~~ and vaccinal strains of ~~the~~ poliovirus.

5. Epidemiological efficacy of mass immunization with live poliovirus vaccine; was for the first time established in the Soviet Union on the basis of information gathered in 1959, this being discussed in detail in our report No.2 (Moscow,1960). Particularly convincing was the reduction in the incidence rate in the Estonian and Lithuanian republics, where triple immunization with live vaccine was effected prior to the onset of the summer poliomyelitis season, as well as in Karaganda and in the Moscow region, where conditions favored comparisons between the groups of the vaccinated and non=vaccinated. In the first quarter of 1960 satisfactory situation with regard to poliomyelitis continued to prevail in the Estonian, Lithuanian and other territories, which were subject to observations. These latter, after their thoroughly controlled investigations gave evidence of a very high epidemiological efficacy of mass immunization with live poliovirus vaccine (incidence=rate of paralytic forms of poliomyelitis reduced 9.5-20.5 times).

Of particular interest are materials covering 1959 vaccination in Tashkent. A synchronous mass inoculation with trivalent live vaccine , carried out at a time of a steep rise in the morbidity rate in Tashkent during 1959 was a definite proof of the possibility to considerably curtail the rate of

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the poliomyelitis incidence within the space of five weeks, this being due to the effect of interference exercised by the vaccinal virus on the epidemiological process and to the rising immunization of susceptible population groups.

In conclusion I should like to point out fruitful international cooperation in the matter concerning live poliovirus vaccine which has set in amongst scientists of the USA, the Soviet Union, Czechoslovakia, Hungary, GDR, Chinese Peole's republic, Bulagaria and other countries on the basis of a broad exchange of scientific information, personal contacts, mutual exchange of end=results of research work and friendly support.

All that has been done heretofore is, undoubtedly, only a promising start of a regular future international cooperation among medical scientists towards speediest eradication of certain infectious diseases or, at least, steep reduction of their incidence.

BIBLIOGRAPHY.

1. A.B. Sabin. Report at the 5th International Conference on live poliovirus vaccine in Washington, 1959.

2. M.P.Chumakov with coll. "On the mass peroral immunization of the population in the Soviet Union with live lopiovirus vaccine from the strains attenuated by A.B.Sabin", 1-77, Moscow, 1960.

3. Chumakov, M.P. with coll. " Problems of vifology", 1959, 5, 520-529, 529-533.

4. Smorodintsev, A.A. with coll. " Bulletin of the World Health Organization", 1959, 20, 1053-1074.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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Study of epidemiologic effectiveness of live attenuated poliovirus vaccine in Byelorussian SSR (preliminary report)

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Analysis of poliomyelitis incidence in Byelorussia for the last decade (1949-1958) reveals two periods: first, 1949-1953, when only sporadic cases of poliomyelitis were reported, and second, 1954-58, when the incidence was rising sharply and reached the peak in 1958 (1000 cases). 314 patients had paralytic form of poliomyelitis. The great majority (95-98 per cent) of cases was in children under 14 years of age, with children under 4 years being mostly affected. By the time immunization with live vaccine was started, poliomyelitis prognosis for 1959 was more favourable than in 1958, but serious enough, however, if judged by shift in poliomyelitis incidence in the first months of 1959. The index of poliomyelitis incidence in 1959 was 1.8 times lower than that in 1958 (the year of the peak incidence), but i.4 times higher than that in 1957.

The examination of data obtained indicates that live attenuated virus vaccination was carried out in 1959 on the background of average poliomyelitis incidence.

Live attenuated poliovirus vaccine (Lot No. 2) prepared at the Virology Department of the Institute of experimental medicine was used. Each child received orally 1 ml (100, 000 TCD_{50}) of the vaccine in a spoonful of 10% sugar syrup, followed by the ingestion of sweet water or tea.

Vaccination program was carried out in the following way: first feeding was with type I monovaccine (542,519 children vaccinated) and second feeding with bi-vaccine consisting of types II and III (532,025 children vaccinated). First feedings were given from April 10 to 25; bi-vaccine feedings were carried out May 10-25. Two feedings with types I+II+III were administered to 503,733 persons. Vaccination program involved children of 6 months

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to 14 years of age in towns, regional centers and large settlements of Byelorussia. Groups of unvaccinated children living in the same towns served as "internal control", and living in rural areas as "external control".

Thorough investigation of all cases of diseases developing during during vaccination program and within one month after it and analysis of their association with vaccination was conducted. On the basis of the evidence obtained conclusion may be made of the complete safety of the live vaccine and absence of any serious reactions among the vaccinated.There were reports of isolated cases (102 per 542,519 vaccinees receiving type I) of fever, mild dispeptic disorders and allergic reactions developing 3-5 days after vaccine ingestion. Distribution of reported reactions among children immunized with live vaccine was not even all over Byelorussia, which makes it impossible to associate many of the reactions with vaccine feedings. Under conditions of large-scale vaccinations occurrence of a number of other diseases is inevitable among groups of population being surveyed. In addition to direct investigation of reactions associated with live vaccine ingestion we analysed the incidence of infectious diseases during the period of vaccination programs. The data obtained indicated the absence of any increase in incidence both of diseases associated with involvement of the central nervous system and of other infections (poliomyelitis, toxic and common dyspepsia, hepatitis, colitis, enteritis, dysentery, pertussis, measles, dyphtheria, scarlet fever, sore throat, influenza and upper respiratory tract catarrhs).

Because of low reactogenicity of the live vaccine and for reasons of greatest coverage of susceptible groups of children a

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question should be raised of maximum reduction of existing contraindications, including certain forms of tuberculosis and of cardiovascular diseases, and large-scale immunization with live poliovirus vaccine should be carried out simultaneously with other vaccination programs.

The examination of serum specimens collected before immunization of children with the live vaccine revealed a significant number of persons without detectable antibody (in 1:4 dilution) to any one or all the three types of poliovirus (seronegative children).

Estimations of susceptible population on serologic evidence (results of pH tests) showed that in the age group of 6 months to 3 years there were 57.5 - 63.2 per cent susceptible children to types I, II and III, in the age-group of 4 to 7 years percentage of susceptible children to types I, II and III was 39.3, 50.0 and 31.1 per cent, respectively; in the age-group of 8 to 14 years 32.3, 41.1 and 12.1 per cent, respectively.

Analysis of paralytic poliomyelitis incidence for the 7 month observation period showed that among the vaccinated children paralytic poliomyelitis was reported only in 3 regions out of 7 and in Minsk. The average annual index of paralytic poliomyelitis incidence among the vaccinated varied in some regions from 1.7 to 3.8. Among the urban unvaccinated children (internal control) it varied from 7.0 to 28.8.

The effectiveness of vaccinations was particularly evident in the age-group of 6 months to 3 years. Among 74,368 vaccinated children there were two cases during 7 months which is 4.5 per 100,000 (average annual rate), while among 77,612 vaccinated

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children of the same age there were 34 cases (74.6 per 100,000). Incidence rate for children of this age in the external control group is 37.3 per 100,000. Thus, poliomyelitis incidence among the vaccinated children of different ages was 16.5 times lower than that among the unvaccinated portion of children in towns and 8.3 times lower than that in rural regions. The index of live vaccine effectiveness is somewhat lower in the age-groups 4-7 years and 8-14 years because of lower and progressively declining incidence in control groups.

The results of the vaccination program were reflected in fundament changes in seasonal poliomyelitis incidence curves. In the first five months of 1959 the curve of poliomyelitis incidence did not differ from the average curve for 5 years, and was even higher in some months. But starting from June (that is, one month after the end of vaccinations) the shape of the curve changed, and the typical seasonal rise in poliomyelitis incidence, like that in previous years, was not observed.

During the years previous to live virus vaccination poliomyelitis incidence among urban population was higher than that among rural population.

In January - April (before vaccination) we observed the usual correlations in the incidence in these two population groups. Vaccinations carried out in April produced changes in these correlations and poliomyelitis incidence among the vaccinated in towns because much lower than in rural regions.

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Results of virologic and serologic surveys of the vaccinated with trivalent live poliovirus vaccine

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Virologic investigations

Determination of frequency of vaccine virus establishment in the intestinal tract of persons vaccinated with live poliovirus vaccine may be used as quality control of the vaccination material, preliminary indication of immunization effectiveness and may be helpful for elucidation of some questions of vaccination process dynamics.

From the paper by M.P. Chumakov et al. it is clear that children under three years of age immunized with monovalent vaccine excreted the virus in 97 per cent of cases on the average, and in the age-group of 20-30 years the virus was found in 22 per cent of cases, that is virus excretion became less frequent with age.

Since in the western regions of the Ukraine immunization was carried out with trivalent vaccine it seemed of interest to follow the vaccination process dynamics with such dosage schedule. For this purpose we selected three children's institutions: one children's home for preschool children (90 persons) half of whom before live virus immunization had been given two injections of Salk vaccine; and two boarding-schools (112 children) where there had been no Salk vaccinations.

Stool specimens were collected one or two days before live virus immunization and after it weekly for two months.

Suspensions of the material collected during a fortnight were prepared, pooled and inoculated into fibroblast tube cultures.

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Table 1

Frequency of vaccine virus excretion in stools from children immunized with trivalent live vaccine

Age-group (years)	Number of children tested	Virus isolated	
		Number	Per cent
3-6	90	58	64.5
	112	50	41

Data in Table 1 show that frequency of vaccine virus excretion was rather high. In children of 3-6 years intestinal carriage was observed in 64.5 per cent, in those of 8-15 years up to 41 per cent.

Serologic survey of 72 first blood specimens collected from children aged 3-6 years before live virus immunization revealed in 30 of the children absence of poliomyelitis antibody to any one or all the three virus types. After immunization 24 (80%) of these 30 children excreted virus. Frequency and duration of virus excretion at different times after vaccination is shown in Table 2.

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Table 2

Duration of virus excretion in children immunized with trivalent live vaccine

Age-group (years)	Number of children tested	Virus excreted at							
		I-II weeks		III-IV weeks		V-VI weeks		VII-VIII weeks	
		No.	%	No.	%	No.	%	No.	%
3-6	90	41	45.5	31	34.4	9	10	1	-
8-15	112	40	35	21	22	8	7	-	-

From the data in Table 2 it is seen that the greatest frequency of virus carriage was observed one and two weeks after vaccination. Thus among pre-school children virus excretion was found in 45.5 per cent; among children of school ages slightly less - 35 per cent. Subsequently there began gradual decline of virus excretion which finally ceased 5-6 weeks after vaccination. In one case type I virus was isolated from pooled specimens collected 7-8 weeks after vaccination.

Observations which were carried out indicate that the vaccine virus spreads to contacts rather soon. In virologic study of 20 children in close contact with vaccinated virus carriage was detected in 8 children: at 3 to 4 week intervals after the beginning of contact in five children and 5 to 6 weeks after the beginning of contact in three children.

Since the immunization was carried out with trivalent

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vaccine it was of interest to follow type distribution of the excreted viruses (Table 3). For that purpose we studied types of viruses isolated at different intervals after vaccination.

Table 3

Type distribution of fecal strains isolated at different intervals after vaccination

Time of survey after vaccination	Number of cytopathogenic agents tested	Virus isolated		
		type I	type II	type III
1-2 weeks	6	1	5	4
3-4 weeks	4	2	2	2
5-6 weeks	1	1	-	-

From the above data it may be seen that in the beginning all the three types of poliovirus were excreted, types II and III slightly more often. In the second month after vaccination type I virus was found most frequently.

It is noteworthy that the children immunized with trivalent vaccine excreted individual types and mixtures of two or even three types simultaneously. Mixtures of types I and III or types II and III were mostly observed.

On the basis of virologic investigations performed it may be stated that good establishment of vaccine viruses is observed in children receiving orally trivalent live vaccine.

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Detection of all three types of poliovirus in stool specimens from vaccinated children leads to the conclusion that interference between viruses, even if it occurs, does not influence the outcome of immunization.

Serologic investigations

Blood specimens were collected before and two months after immunization with trivalent live vaccine for determination of rise in antibody titers.

Blood specimens were stored in lo-temperature refrigerators and paired bloods were tested simultaneously. Before use sera were teated at 56°C for 30 minutes and diluted 1:2, that is, first dilution after addition of the virus was 1:4. Sera were tested in neutralization tests against 100 TCD_{50} of each virus.

Results of tests with 64 paired serum specimens are presented below.

Table 4

Rise of antibody titers two months after immunization with trivalent live poliovirus vaccine

Antibody titer before immunization	Rise in titer of antibody to types					
	I		II		III	
	number	number of sera tested	number with rise in titer	number of sera tested	number with rise in titer	number with rise in titer
4	23	23	9	9	14	14
4-8	16	14	14	14	20	19
16-32	15	14	19	18	18	15
64-128	8	6	13	13	9	5
256 +	2	1	9	4	3	1

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From the data in Table 4 it is seen that in those cases where prevaccination antibody levels had been low or negative rise of antibody titers after vaccine feeding was observed in 100 per cent. In those cases where prevaccination antibody titers were high (64 and over) rise of antibody titers was observed much more rarely.

Table 5 presents data on rise of antibody titers to individual virus types.

Table 5

Rise of antibody titers to individual virus types
2 months after ingestion of trivalent live vaccine

Prevaccination titers of antibody to individual wirus types		Antibody titers after immunization									Number of sera tested
		14	4	8	16	32	64	128	256	512	1024	
Type I	256 +								1		1	2
	64-128						2	3	3			8
	16-32					1	5			2		15
	4-8			2	1	3		4	1	3	2	16
	4			1	3	1	3	3	5	5	2	23
Type II	256 +								4	2	3	9
	64-128							2	4	4	2	13
	16-32				1	2	6	4	3	2	1	19
	4-8					2	3	1	3	2	3	14
	24						3	1	1	1	3	9
Type III	256 +								2	1		3
	64-128					1			2	1		9
	16-32					4	7	5	1			18
	4-8					4	7	5	3	1		20
	4						6	4		3	1	14

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From the data in Table 5 it is seen that in the majority of sera tested antibody titers increased considerably.

The greatest increase of antibody was observed in those cases where prevaccination antibody titers had been either low or negative. This is confirmed by data in Table 6 which shows the rate of increase in antibody titers in sera with different levels of immunity before vaccination.

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Table 6

Rate of increase in antibody titers in the vaccinated 2 months after immunization with trivalent live vaccine x)

Prevaccination antibody titers		Titers unchanged	Rate of increase in postvaccination antibody titers										Number of sera tested
			2	4	8	16	32	64	128	256	512	1024	
Type I	256 +	1	1										2
	64-128	2	4	2									8
	16-32	1	1	6	5		1	1					15
	4-8	1	1	1		3	1	3	3	5	5	2	16
	4				1	3	1	3	3	5	5	2	23
Type II	256 +		5	1									
	64-128		5	4	3	1							13
	16-32	1	3	9	1	3	1	1					19
	4-8				2	3	4		1				14
	4							3	1	1	1	1	
Type III	256 +	2		1									3
	64-128	4	3	2									9
	16-32	3	7	6	2								18
	4-8	1		1	7	6	4	1					20
	4							6	4	3	1		14

x) For calculation of the rate of increase in antibody titers 4 titer was equated to 1.

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Data in Table 6 show that antibody rise was observed in the majority of children tested, but the increase in titer was not uniform. In sera with negative or low prevaccination antibody levels the titer increased 128-fold or more while in sera with high levels of prevaccination antibody the titer increased 2-4 fold if at all.

Great increase of antibody titers in the vaccinated is an undoubtful proof of high immunogenic potency of the vaccine. Considering the fact that immunization was carried out with trivalent vaccine and rise of antibody to all three types of poliovirus has been observed, trivalent vaccine may be recommended for large-scale immunization of population. The problem of interference in immunization with trivalent live vaccine needs further investigation.

The data we obtained confirm the conclusion made by Prof. M.P. Chumakov and co-workers that interference even if it occurs has no significant influence on production of immunity.

Conclusions

1. The investigations performed demonstrated good establishment of vaccine viruses in immunized persons. Frequency of excretion of virus in children aged 3-6 years was 64.5 per cent, in schoolchildren 41 per cent. Virus carriage was observed in 80 per cent of children without prevaccination antibody.

2. Great increase of antibody titers to all three types of poliovirus in the majority of immunized with trivalent live vaccine indicates high immunogenic potency of the vaccine. The data obtained allow to recommend trivalent live vaccine for use in large-scale immunization programs.

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Changes in the Central Nervous System of Monkeys Infected with the Poliovirus Strains of the III type , which were Isolated from the Feces of Vaccinated Cildren

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I. A possibility of the restoration and augmentation of the neurotropic properties (reversion) of the attenuated poliovirus strains after passing them through the human body was one of the principal problems discussed before the onset of a large-scale vaccination with the live poliovirus vaccine in the U S S R. The actuality of this problem persists as yet.

2. The solution of a problem on reversion may be found only in experimental studies, however, during the evaluation of experimental data, we are obliged to discount the possibility of a viral combination of the attenuated strains with the noxious ones.

3. In the pathohistological laboratory of the Institute on Poliomyelitis Research, as well as in the other laboratories, we were able to estimate some peculiarities of the morphological changes found in the nervous system of monkeys infected with the attenuated strains of poliovirus. To some extent, this gives a possibility to differentiate morphologically the manifestations of residual neurovirulence, caused by the attenuated poliovirus strains from the infection provoked by a combination of attenuated strains of poliovirus with the street virus strains, becoming such in the process of their passages through the human alimentary canal.

4. Our material was recieved from the laboratory of the Institute for Poliomyelitis Research of the Academy of Medical Sciences of the U S S R, where it was studied virologically.

We have studied the central nervous system of 26 monkeys infected intracerebrally with the poliovirus of the III type (third sample of live vaccine prepared in the institute), isolated from the feces of 3 children vaccinated with the

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live poliovaccine. The virus was isolated from the feces on the 3rd, I0th, 2Ist and 30th day following vaccination.

For the purposes of comparison we have investigated the central nervous system of I4 monkeys infected with the attenuated poliovirus strains introduced intracerebrally and attributed to the same virus sample (III type of poliovirus).

5. In the central nervous system of the I4 monkeys infected intracerebrally with the attenuated poliovirus strains of the III type we were not able to distinguish any morphological changes characteristic for poliomyelitis. Clinical symptoms of the disease in these cases were absent.

6. Of the 26 monkeys,infected with the virus isolated from the feces of vaccinated children, in the central nervous system of 6 we have revealed the morphological changes characteristic for poliomyelitis.

In 5 of these 6 cases the morphological manifestations have corresponded to the changes, pathognomonic for the infection of monkeys caused by the attenuated poliovirus strains (aparalytic form of poliomyelitis). In these cases the clinical signs of the disease were also absent. The extent of the morphological changes had varied from very mild to a quite significant.

In one case , when the virus was isolated from a child (Kamensky) on the I0th day following vaccinatin, the morphological changes were very severe. Clinically, this case was considered as a paralytic form of poliomyelitis.

On comparison with the viruses isolated from the other children, the virus isolated from the feces of Kamensky caused relatively more extended and more profound changes in the central nervous system.

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7. Our materials, although not very numerous, allow to say, that during the passages of virus through the children, it is possible, in a small percent of the cases, to detect some augmentation of the viral neurotropism, which is manifested by the morphological changes in the central nervous system pathognomonic ~~to the~~ for the attenuated strains of poliovirus.

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ANTIBODY RESPONSE IN CHILDREN IMMUNIZED WITH TRIVALENT LIVE VACCINE FROM A.B.SABIN'S STRAINS

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Simultaneous use of three immunologic types of attenuated strains for mass oral poliomyelitis immunization allows to vaccinate large population groups against all three types of poliovirus in a short time with most complete involvement.

It is believed, however, that serological response to trivalent vaccine may be lower than that in separate immunization with monovaccines due to interference between vaccine strains. Therefore further accumulation and examination of serological data are necessary.

Serological survey of children vaccinated during winter, 1959, with trivalent live vaccine from sabin strains in Estonian and Lithuanian SSR (Dobrova, Yankevich, Chumakov et al., 1959) demonstrated sufficiently regular antibody response to the three poliovirus types in 66.7 to 88.6 - 89.0 per cent of children without prevaccination antibody to one or more types of poliomyelitis virus. The results varied, however, in different observations. It would be of interest to determine factors which affect serologic response.

In May-June and July, 1959, trivalent live vaccine was used for mass immunization of children in Karaganda and Moscow regions. This paper presents the results of serologic surveys of children vaccinated in summer in towns and settlements of Moscow region and in three towns of Karaganda region.

Materials and Methods

Children of 2 months to 15 years of age were immunized orally with a mixture of monovaccines prepared at the Institute for Poliomyelitis Research from Sabin attenuated strains of

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the three poliovirus types. The vaccine was diluted immediately before use so that two drops contained 100,000 TCD_{50} of each strain. Practically to 7 ml of the diluent 1 ml of monovaccine of each type was added. The vaccine was given to children in a spoonful of water or tea followed by ingestion of water. The vaccine was fed twice with 1-1 1/2 month interval. Venous blood was collected before, 1-1 1/2 months after first and 1-1 1/2, 3, 4 and 6 months after second feeding. In February, 1960, children received type I monovaccine and one month later trivalent vaccine in draged-candy. Two weeks later the children were bled. Altogether 841 children mainly of 6 months to 4 years of age were tested.

In Moscow region (see Table 1) serum specimens were collected from 425 children, of them 255 living in Ukhtomsk, Kuntsevo, Reutovo, Balashikha and Khimki districts, in towns of Lyublino, Perovo, Electrostal, Babushkin and Volokolamsk. These children had not been vaccinated with killed vaccine. 170 serum specimens were obtained from children in three children's homes. 94 serum specimens were collected from children under two years of age.

In Karaganda region 416 children from towns of Karaganda Balkhash and Osokarovka were examined before vaccination.

Tables 2 - 4 present data on the lack of antibody to polio viruses and numbers of children with different antibody patterns to the three poliovirus types in Moscow and Karaganda regions.

As is seen in the Tables, of 425 children in Moscow regi before vaccination 188 (44.2%) had no type I antibody, 133

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(31,3%) no type II antibody and 208 (48.8%) no type III antibody to poliovirus. 85 children (20.0%) were triple-negative, 160 children had antibody to all three poliovirus types. Of other antibody patterns most often antibodies to type II alone were found (14.1%) or to types I and II (10.8%). Very seldom (only in 1.7%) were only type III antibodies present. In children under 1 year of age 20 sera of 33 tested had no antibody to any of poliovirus types, and only 3 sera neutralized type II poliovirus. Among children of 1 to 2 years there were 20.6 per cent triple-negatives, of 2 to 3 years 12.8 per cent, of 3 to 7 years 5.9 per cent. All 39 children of 7 to 10 years of age had poliomyelitis antibody, of them 25 to all the three types of poliovirus.

Of 416 children in Karaganda region (see Table 4) 97 (23.6%) had no type I antibody, 71 (17.1%) no type II antibody and 99 (23.8%) type III antibody. 24 (5.8%) children were triple-negative. In the age-group under 1 year 46.6 per cent of children had no antibody to any type of poliovirus. Both in Moscow and Karaganda regions percentage of children possessing type II antibody increased with age. The highest per cent of sera with type I and type III antibody was found in the age-group of 7 to 10 years. It may probably be connected with the first epidemic season of 1955 when children, then 1 - 3 years old, were infected to a greater extent than older children. In the age-group of 10 to 15 years 4.8 per cent of children were triple-negative, 28.6 percent had no type I antibody, 11.9 per cent - type II and 19.0 per cent had no type III antibody (Moscow region, Table 2).

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Serological investigations were carried out mainly by pH neutralization tests in tubes or insulin vials. A portion of sera was tested by the cytopathogenic neutralization test. Besides, some sera were tested in parallel by complement-fixation tests and precipitation tests in agar gel on slides. Serum specimens from each child (2-6 specimens) were always examined simultaneously in one test.

Results

Examination of sera from 223 children with prevaccination lack of antibody to some types by pH neutralization test showed that one month after feeding with trivalent live vaccine some children responded with antibody development to all three types, and others to two or one type of poliovirus. Of 142 children without prevaccination type I antibody 92 (64.8%) acquired antibody to this type. Of 106 children without type II antibody before vaccination 85 (80.2%) developed it. Smaller number of children responded with type III antibody development (86 of 151, or 56.9%). Of 60 triple-negative children 27 (45.0%) developed each type I and type III antibody, and 43 (71.7%) - type II antibody.

Percentage of children with prevaccination antibody increased by 39.9% for type I, 35.4% for type II and 35.9% for type III.

These results are definitely lower compared to those obtained by Dobrova, T.H. in Estonian SSR after immunization with trivalent vaccine in winter-spring season (see Table 6). As is shown in another communication from our laboratory, in Moscow and Karaganda regions, where vaccinations had been carried out

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in summer time, establishment of vaccine strains was prevented by extremely wide dissemination of nonpoliomyelitis enteric viruses during this period. In favour of possible inhibiting influence of enterovirus season is the fact that the least satisfactory results were obtained in children's homes Lu. and R. where considerable extent of ECHO and Coxsackie virus carriage had been found (Table 6). Materials on interference between vaccine strains and nonpoliomyelitis enteric viruses are discussed in a separate communication.

And yet, despite the unfavourable effect of enteric virus carriage, one feeding of trivalent live vaccine resulted in significant changes in antibody patterns compared with prevaccination status in that 128 children of 223 seronegatives converted to triple-positives. 51 of 60 triple-negative children developed antibody to one or more types of poliomyelitis viruses, and only 9 children remained triple-negative (Table 7, fig.1).

Best results in regard to increase in the percentage of children with antibody to all the three types were observed in children from different towns and settlements of Moscow region (68.4%) previously not vaccinated with killed vaccine (Table 8). In Karaganda region per cent of triple positive children increased by 56.5%, while in children's home L. in Moscow region only by 23.1%. Summary data on the increase in the number of children with antibody to all the three types of poliovirus vaccinated during summer were only 4.6% lower than those obtained in winter vaccination with trivalent vaccina (Estonian SSR, data by Dobrova, I.N.). The increase in

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the number of children developing type II antibody differed from that observed in winter only by 5.4%. A greater difference between the number of children developing antibody after vaccination in winter and in summer was observed for type I and type III antibody (17.2 and 9.0 per cent, respectively).

Table 9 presents antibody titers in children without prevaccination homologous antibody. It may be seen, that type I antibody developed most often in titers 1:16 - 1:64; 25% of children developed type II antibody titers of 1:256 or greater. The lowest titers after one feeding were observed with type III antibody: half of the children had type III antibody in titers 1:16.

Analysis of age-distribution of antibody (Table 10) showed that one month after one feeding of trivalent live vaccine types I and III antibody were produced in a higher portion of older children: 33.3% of type I - negative and 27.8% of type III - negative children acquired antibody. The corresponding figures for children of 1 to 3 years old were 50.0% and 36.0%, respectively, for children of 3 to 7 years - 87.7% and 75.5%, respectively, for children of 7 to 14 years - 94.1% and 78.9%, respectively. It is possible that children of older age-groups have had previous poliomyelitis infection experience which was not manifested by the development of antibody detectable by the pH test.

At the same time one must take into account the fact that younger children are more exposed to infection with enteric viruses which evidently prevented good immunologic response to vaccine strains fed in summer.

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In contrast, type II antibody developed in 80.0% of children under one year of age. The impression is that younger children are more susceptible to type II virus or that type II virus is less inhibited by "wild" enteroviruses present in the intestinal tract. Type II antibody developed in 56.7% of children aged 1 - 3 years, in 97.3% of children of 3 - 7 years, and in 94.1% of children of 7 to 14 years.

Refeeding trivalent live vaccine one month later did not result in considerable improvement of the results obtained after first feeding. While in L. children's home the percentage of children acquiring type I antibody after one feeding did not change one month after refeeding, in Karaganda even some decrease was found in numbers of sera with low titers which was reflected, though not considerably, in summary results (decrease by 3.8 per cent). In groups of children without prevaccination type II antibody both in L. children's home and in Karaganda region there was some increase in per cent of children developing type II antibody (11.8%). Greater changes were observed in increase of type III antibody, especially in L. children's home (from 28.9% after first feeding to 48.5% after refeeding). Probably, by the time of refeeding the intestinal virus carriage preventing type III vaccine strain multiplication had reduced, which led to more extensive multiplication of vaccine strains and produced further rise in antibody levels. This was reflected in general antibody rise by 16.4% (Table 11).

Comparison of the results observed one month and 3 - 4 months after two feedings with trivalent live vaccine from

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Sabin strains reveals a certain reduction in the percentage of children acquiring type I antibody (by 10.5%) and a small increase to type II (by 3.4%) and type III (by 2.6%) poliomyelitis antibody (Table 12).

The lack of significant improvement of the results at later periods and even a certain reduction of type I antibody is evidently related to drop in titers in cases of incomplete immunity as a result of interference by enteric viruses and of reduced opportunity for contact transmission of type I and type III viruses inhibited by type II vaccine virus multiplication. As surveys of vaccine contacts showed, they had predominantly type II virus carriage accompanied by antibody production. Thus, the children were deprived of additional immunization with types I and III poliovirus vaccine.

Conclusions

1. One feeding with trivalent live poliovirus vaccine carried out during summer months in Moscow region and Karaganda produced antibody rise, somewhat lower to types I and III in comparison with the type II antibody rise. As is shown in another communication, in these regions of trivalent vaccination programs some inhibition of intestinal multiplication of types I and III vaccine viruses was observed in summer months (shortened and irregular multiplication), probably due to interference by enteric viruses having a very wide dissemination.

2. Under these conditions type II vaccine strain (in trivalent mixture) was found to be most capable to overcome interference by enteroviruses and even, in its turn, to inhibit type I and III vaccine strains.

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3. Despite unfavourable conditions for vaccination, significant changes in antibody patterns were observed already one month after trivalent vaccine feeding. Thus, only 9 children (15%) of 60 formerly triple-negatives have not responded to vaccination. 128 children of 223 with prevaccination antibody deficiency developed antibody to all three types of poliomyelitis virus.

4. In children immunized with trivalent live vaccine type I antibody developed most often in titers of 1:16 to 1:64. In 25% of children type II antibody titers were greater than 1:128. In half of the children type III antibody titers did not exceed 1:16. Consequently antibody response evaluated by titers was also best for type II.

5. Lower percentage of youngest children developed type I and type III antibody compared to older children. In contrast, type II antibody were produced in sufficiently high per cent of children under one year (80.0%).

6. Refeeding of trivalent live vaccine one month after first feeding produced considerable boost of type III antibody developed after first feeding but had no effect on type I and type II antibody levels.

7. All the above findings indicate that administration of trivalent vaccine in summer months under conditions of almost inevitable high extent of interference by nonpoliomyelitis enteric viruses and wild poliovirus strains is justified and, under these conditions may be more perspective than separate administration of monovaccines.

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Table 1

Age-distribution of children from whom serum specimens were collected in Moscow region

	Total number of children	Age					
		0-11m	1 yr.	2 yr.	3-6	7-9	10-15
Towns and districts	255	5	15	24	130	32	42
Children's home Lu.	78	15	24	9	30		
Children's home R.	65	3	24	30	15		
Children's home Lyt.	27	-	8	2	10	7	
Total	425	23	71	65	185	39	42
Per cent	100.0	5.4	16.7	15.3	43.5	9.2	9.9

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Table 2 - Absence of poliomyelitis antibody in children of different ages before vaccination (Moscow region, 1959).

Age-group (years)	Number of sera tested	Number of sera without antibody to type I		type II		type III		Triple-negative sera	
		No.	%	No.	%	No.	%	No.	%
0-I	23	23	I00.0	20	86.0	23	I00.0	20	86.0
I-2	7I	59	83.I	50	70.4	63	88.7	43	60.6
2-3	65	5I	78.6	I7	26.2	50	76.9	9	I3.8
3-7	I85	4I	22.2	34	I8.4	58	3I.4	II	5.9
7-I0	39	2	5.I	7	I7.9	6	I5.4	-	-
I0-I5	42	I2	28.6	5	II.9	6	I9.0	2	4.8
Total:	425	I88	44.2	I33	3I.3	208	48.8	85	20.0

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Table 3 -

Antibody patterns in children before immunization with trivalent live vaccine. Moscow region.

Age-group (years)	Number of sera tested	Antibody to three types of poliovirus													
		000		00+		0+0		0++		+00		+0+		++0		+++	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0-I	23	20	86.0	-	-	3	I4.0	-	-	-	-	-	-	-	-	-	-
I-2	7I	43	60.6	I	I.4	I4	I9.7	I	I.4	4	5.6	2	2.8	2	2.8	4	5.6
2-3	65	9	I3.8	I	I.5	28	43.I	3	4.6	6	9.2	I	I.5	7	I0.7	I0	I5.4
3-7	I85	II	5.9	4	2.2	I0	5.4	I6	8.6	7	3.2	I2	6.5	30	I6.2	95	5I.3
7-I0	39	-	-	-	-	I	2.6	I	2.6	-	-	7	I7.9	5	I2.8	25	64.I
I0-I5	42	2	4.8	I	2.4	4	9.5	5	II.9	-	-	2	4.8	2	4.8	26	6I.9
Total	425	85	20.0	7	I.6	60	I4.I	26	6.I	I7	4.24	5.6		46	I0.8	I60	37.6

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Table 4 - Absence of poliomyelitis antibody in children of different ages before vaccination (Karaganda, 1959)

Age group (years)	Number of sera tested	Number of sera without antibody to Type I No.	Type I %	Type II No.	Type II %	Type III No.	Type III %	Triple-negative sera No.	Triple-negative sera %
0-I	I5	8	53.3	7	46.6	9	60.0	7	46.6
I-4	236	66	28.0	43	I8.2	75	3I.8	I7	7.2
5-7	I20	I8	I5.0	I9	I5.8	I4	II.7		
8-I0	22	2	9.I	I	4.6				
II-I4	20	3	I5.0	I	5.0	I	5.0		
I5+	3								
Total	4I6	97	23.3	7I	I7.I	99	23.8	24	5.8

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Table 5 - Antibody response one month after one feeding with trivalent live vaccine from Sabin strains in children of 3 months to I5 years of age with prevaccination antibody deficiency (summary data for Moscow and Karaganda regions).

Prevaccination	No. of children	One month after one feeding								Total with antibody to types		
		000	00♦	0♦0	0♦♦	♦00	♦0♦	♦♦0	♦♦♦	I♦	II♦	III♦
000	60	9	4	I4	6	3	I	7	I6	27 45.0	43 7I.7	27 45.0
00♦	I2	-	I	-	2	-	-	-	9	9	II	I2
0♦0	37	-	-	8	I	I	-	5	22	28	36	23
0♦♦	33	-	-	-	5	4	-	I	23	28	29	28
♦00	7	-	-	-	-	-	-	2	5	7	7	5
♦0♦	27	-	-	I	-	-	3	-	23	26	24	26
♦♦0	47	-	-	2	-	-	I	I4	30	45	46	3I
Total	223	9	5	25	I4	8	5	29	I28	I70 76.2	I96 87.2	I52 68.2

Of them possessed antibody:

I♦ 8I - 36.3%

II♦ II7 - 52.5%

III♦ 72 - 32.3%

Acquired antibody additionally:

39.9%

35.4%

35.9%

Before vaccination	Number of children without antibody	Antibody developed I month after one feeding		
		Type	Number	Per cent
$I^0II^0III^0$	60	I	27	45.0
		II	43	7I.7
		III	27	45.0
I♦	I42	I	92	64.8
II^0	I06	II	85	80.2
III^0	I5I	III	86	56.9

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Table 6 - Antibody response in seronegative children one month after one feeding with trivalent live vaccine

	Antibody development in groups of "negative" children											
	I°		II°		III°		I° II° III° type I			type II		type III
	No.	%	No.	%	No.	%	No.	%		No.	%	No. %
Moscow region (towns and districts)	57/78 x)	73.1	82/92	89.1	60/86	69.8	I9/3I	6I.3		24/3	77.I	I8/3I 58.I
L.children's home	I0/32	50.0	I5/20	75.0	II/38	28.9	7/I9	36.8		I5/I9	78.9	4/I9 2I.0
Karaganda region	I9/32	59.4	I5/22	68.2	I5/27	55.5	I/I0	I0.0		4/I0	40.0	5/I0 50.0
Moscow and Karaganda regions (summary data)	92/I42	64.8	85/I06	80.2	86/I5I	56.9	27/60	45.0		42/60	7I.7	27/60 45.0
Estonian SSR (data by Dobrova,I.N.)	28/39	7I.8	20/24	83.3	8/30	73.3	8/I3	6I.5		I0/I3	76.9	I0/I3 76.9

x/ 57/78 - 57 of 78 children formerly type I negative; developed type I antibody.

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Table 7 - Antibody patterns before vaccination and one month after one feeding with trivalent live vaccine from Sabin strains in 223 children with antibody deficiency

	Before vaccination		One month after	
	No. of children	Per cent	No. of children	Per cent
000	60	26.9	9	4.0
00♦	I2	5.4	5	2.2
0♦0	37	I6.6	25	II.2
0♦♦	33	I4.8	I4	6.3
♦00	7	3.I	8	3.6
♦0♦	27	I2.I	5	2.2
♦♦0	47	2I.I	29	I3.0
♦♦♦	0	0	I28	57.3

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Table 8 - Increase in the number of children possessing antibody to the three types of poliovirus one month after one feeding with trivalent live vaccine

	Number of children	Increase of numbers of children with antibody							
		to 3 types		to type I		to type II		to type III	
		No.	%	No.	%	No.	%	No	%
Moscow region (towns and districts)	I33	9I	68.4	57	42.9	78	58.7	55	4I.4
L. Children's home	39	9	23.I	I6	4I.I	I6	4I.0	I2	28.I
Karaganda region	5I	28	54.9	I6	3I.4	I3	25.3	I3	25.5
Moscow and Karaganda regions (summary data)	223	I28	56.6	89	39.9	79	35.4	80	35.9
Estonian SSR (data by Dubrova, I.N.)	49	30	6I.2	28	57.I	20	40.8	22	44.9

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Table 9 - Antibody titers in children developing antibody one month after one feeding with trivalent live vaccine

Serum dilution	Antibody development to:					
	Type I		Type II		Type III	
	No. of children	%	Number of children	%	Number of children	%
I:4	7	8.4	I	I.2	8	I0.4
I:8	9	I0.8	I2	I4.3	7	9.I
I:I6	I6	I9.3	I3	I5.5	24	3I.I
I:32	I8	2I.7	I4	I6.7	I5	I9.5
I:64	9	I0.8	I7	20.2	7	9.I
I:I28	I7	20.5	6	7.I	II	I4.3
1:256 and greater	7	8.4	2I	25.0	5	6.5
Total :	83	I00.0	84	I00.0	77	I00.0

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Table 10 - Antibody response one month after one feeding with trivalent live vaccine in children without prevaccination homologous antibody by ages (Moscow and Karaganda regions)

Age-groups (years)	Total number of children	Antibody response to								
		Type I			Type II			Type III		
		No. of children	acquired antibody	%	No. of children	acquired antibody	%	No. of children	acquired antibody	%
0-1	18	18	6	33.3	15	12	80.0	18	5	27.8
1-3	70	56	28	50.0	37	21	56.7	61	22	36.0
3-7	95	45	43	87.7	37	36	97.3	53	40	75.5
7-14	40	19	15	94.1	17	16	94.1	19	15	78.9
Total	223	142	92	64.8	106	85	80.2	151	86	56.9

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Table 11 - The effect of refeeding with trivalent live vaccine from Sabin strains on antibody response

Time after vaccination	Antibody response to								
	Type I			Type II			Type III		
	Total no. of children I°	Acquired antibody	%	Total no. of children II°	Acquired antibody	%	Total no. of children III°	Acquired antibody	%
Lu. children's home									
1 month after first feeding	32	I6	50.0	20	I5	75.0	38	II	28.9
1 month after second feeding	30	I5	50.0	22	I8	8I.8	33	I6	48.5
Karaganda region									
1 month after first feeding	32	I9	59.4	22	I5	68.2	27	I5	55.5
1 month after second feeding	27	I4	5I.8	I8	I4	77.8	29	I9	65.5
Total									
1 month after first feeding	64	35	54.7	44	30	68.2	65	26	40.0
1 month after second feeding	57	29	50.9	40	32	80.0	62	35	56.4
Difference			-3.8			+II.8			+I6.4

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Table 12 - Antibody response one and three to four months after two feedings with trivalent live vaccine from Sabin strains

Time after vaccination	Antibody response to								
	Type I			Type II			Type III		
	Total no.of children I^0	acquired antibody	%	Total no.of children II^0	acquired antibody III^0	%	Total no.of children III^0	acquired antibody	%
R.children's home									
1 month	38	22	57,9	16	15	93.7	41	11	26.8
4 months	37	18	48.6	12	11	91.6	38	13	34.2
Karaganda region									
1 month	32	19	59.4	22	15	68.2	27	15	55.5
3 months	15	7	46.6	8	6	75.0	11	7	63.6
Total:									
1 month	70	41	58.6	38	31	81.6	68	26	38.2
3 - 4 months	52	25	48.1	20	17	85.0	49	20	40.8
Difference			- 10.5			+ 3.4			+ 2.6

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INSTITUTE FOR POLIOMYELITIS RESEARCH

STAT

Evaluation of Different Methods of Neutralizing Antibody Estimations Used in Poliomyelitis

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Neutralizing antibodies in poliomyelitis are estimated mainly by two methods: the cytopathogenic test (CPT) in tubes and the pH test in tubes or plastic panels. Simultaneous use of both tests has frequently given different results. Antibody titres estimated in the pH test are usually higher, and in some instances pH antibodies can be demonstrated even when the result of CPT is negative. In this connection Sabin (1) speaks of low avidity (pH) antibodies and high avidity (CP) antibodies and suggests that the main reason for this discrepancy is a qualitative difference in the antibody character developing in the course of poliomyelitic infection.

Because this conception is not generally accepted and its theoretical aspects are widely discussed, we shall try to review and evaluate our experience gained in extensive serological studies undertaken in Czechoslovakia in 1958 and 1959 in connection with a field trial with live poliomyelitis vaccine (Sabin).

M a t e r i a l

The results which are presented in this paper are based on the investigation of following materials:

Material A

The sera investigated in serological surveys were sampled at random in two Czech regions, where most the children aged 2 - 8 years were vaccinated with live poliovirus vaccine (2). The first sampling was performed in November, 1958 about one month before vaccination with type 1 was started, the second sera were sampled in March, 1959, approximately 1 month after type 2, two months after type 3 and about 3 months after type 1 was fed. The second

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sera were not taken from the same persons as the first sera. All serum specimens were tested in pH and CP tests simultaneously.

Material B

114 paired sera from children aged 2 - 8 years vaccinated with the three types of live poliovirus vaccine were investigated in both tests. Most of these children were chosen at random, the rest of the paired serum specimens were obtained from children followed up in special family study. The first and second sera were collected in the same time intervals as in Material A, i.e. approximately 1 month before the first dose and 1 month after the last dose of vaccine.

Another series of 238 of paired serum specimens were obtained from children vaccinated with the fourth dose of Salk vaccine (1 ml subcutaneously). The first serum samples were drawn immediately before the injection and the second a fortnight later.

Material C

In order to gain more and deeper informations on the dynamics and character of poliomyelitis neutralizing antibody development, the following experiment was performed: a group of young adults aged 15 - 18 years were fed with about 100,000 TCD_{50} of type 3 attenuated poliovirus (strain Leon 12 $a_1 b$). Blood samples were taken before feeding and then on the 4th, 7, 10, 14, 21, 28, 35, 42nd and 84th day after it. In the same time intervals stool specimens were taken and virus excretion was followed up.

Methods

In the investigation of Materials A and B the CPT and pH test were performed by means of the conventional technic with 100 TCD_{50}

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of virus and one hour incubation of the virus-serum mixture at room temperature. The strains Brunhilde, MEF_1 and Sauckett were used.

Cytopathogenic test: tube tissue cultures from versenated monkey kidney cells were inoculated with 0.2 ml of the mixture of virus and serum diluted 1/4 for the purposes of the serological surveys, and, when investigating the antibody response in paired sera, 1/4 to 1/1024, in fourfold steps. Every dilution of serum was tested against every type of poliovirus in one tube. The results were read on the 5th day.

pH test: this test was carried out in polystyrene panels. The sera were investigated in dilutions 1/4 to 1/256 for the serological surveys, and, when following the antibody response in paired sera, 1/4 to 1/1024 in fourfold steps. The virus-serum mixtures in an amount of 0.4 ml were covered with paraffin oil,and after one hour incubation at room temperature 0.2 ml of cell suspension, containing 25,000 of versenated monkey kidney cells was added. Parker's medium in Hanks' solution with 0.3% of glucosis and 5% of monkey serum, previously tested for the absence of polioviruses inhibitors, was used. Every dilution of serum was tested against every type of virus in one cup.

In the study of antibody development (Material C) the following methods of neutralizing antibody estimations were used:

a) the conventional CPT with 100 TCD_{50} of virus and one hour incubation of the virus-serum mixture at room temperature,

b) CPT with 100 TCD_{50} of virus and 6 hour incubation at 37° C and overnight at +4° C,

c) pH test with 100 TCD_{50} of virus and one hour incubation at room temperature,

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d) pH test with 100 TCD_{50} of virus and 6 hour incubation at 37°C and overnight at + 4°C,

e) immuno-inactivation test (IIT) with 10 TCD_{50} of virus and 6 hour incubation at 37°C and overnight at +4°C, as recommended by Sven Gard (3).

Testing by all the above methods was performed simultaneously from the same virus and serum dilutions for every individual case. In this study we used the strain Leon 12 a_1 b instead of Sanckett. The sera were diluted in fourfold steps from 1/4 to 1/1024 (in IIT up to 1/4096). Three tube cultures in CPT, two cups in pH tests and 10 tube cultures in IIT were used per one dilution of serum. The titers were calculated according to Kärber's method. The investigation is not yet completed and detailed results will be published later. We shall only briefly mention some results obtained in studying the homotypic antibody response, which are directly related to the problem under discussion.

Results

In Fig. 1 and 2, and in Tab. 1 there are reviewed the results of serological surveys performed in the general population of two Czech regions.

The figures show that the most sera antibodies were demonstrated simultaneously in both conventional pH and CP tests. In a portion of sera only pH antibodies were found; on the other hand, CP antibodies in absence of pH antibodies were demonstrated only rarely.

Table 2 presents the number of sera investigated in defined age groups, the number of sera positive in at least one test used (so called immune persons), and from the later number the percen-

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tage of persons in which only pH antibodies were demonstrated in absence of CP antibodies. The table shows:

1) from the group of so called immune persons the percentage of individuals possessing pH antibodies only is 9.5 for type 1, 8.3 for type 2 and 16.1 for type 3;

2) the highest percentage of so called immune persons having pH antibodies only is in the youngest age group of infants aged up to 6 months, with predominantly maternal antibodies. This finding is in sharp contrast to a relatively low incidence of pH antibodies only among immunes at the age of 20 and over, i.e. the age of most of the mothers.

In table 3 children younger than 6 months are divided in one month age subgroups. The table shows that in the youngest subgroup the percentage of individuals who have pH and have not CP antibodies is relatively low and approaches nearest to the incidence of pH and CP antibodies in adults over 20 years.

The results of the investigation of antibodies in paired serum specimens are in Tables 4, 5, 6 and 7.

From the comparison of antibody response determined in pH and CPT it can be seen:

1) in children without pre-existing homologous seroimmunity (Group 1, Table 4) the antibody response to type 1 and 3 was demonstrated more frequently in pH than in CP test. This difference was more evident in children vaccinated with the fourth dose of Salk vaccine than in children fed with live attenuated polioviruses. The frequency of antibody response to type 2 was approximately the same in both tests;

2) in children with a low pre-existing homologous seroimmunity, with antibodies demonstrable only in pH test (Group 2,

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Table 5), vaccinated with the fourth dose of Salk vaccine, much smaller differences between the antibody responses measured in pH and CP test were found than in children without pre-existing homologous sero-immunity (Group 1). The antibody response to type 1 and 2 was found a little more frequently in CP test than in pH test.

In children vaccinated with the Sabin vaccine the ratio between the frequency of antibody response in pH and CP test was almost the same as in children without pre-existing homologous immunity.

3) In children with "solide" pre-existing sero-immunity, with antibodies demonstrable in both pH and CP tests (Group 3, Table 6), the antibody rises both after the fourth dose of Salk vaccine and the live poliovirus vaccine were more frequent in CP test than in pH test.

The data of the antibody development measured by the different methods of neutralization tests, in young adults fed with the 100,000 TCD_{50} of type 3 attenuated virus, are given in Fig. 3 and 4.

Fig. 3 shows that in 5 of 6 until now investigated cases without pre-existing homologous seroimmunity, antibodies appeared earlier and reached higher titers in the CP test with 6 hour incubation, in the pH tests with 1 and 6 hour incubation and in IIT, than in conventional CPT with 1 hour incubation of the virus-serum mixture. The antibody levels estimated in CPT with 6 hour incubation were in most cases significantly lower than in pH tests; titers found in IIT were in all cases higher than in CPT with 6 hour incubation, but lower or on the same level as in pH tests. The highest differences in antibody titers estimated by

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different tests were found in the first phases of antibody development. In the further course these differences became lower in some cases. After the fourth week, when the pH antibodies reached their highest levels, they began to drop, while still later a small increase of CP antibodies could be observed.

On the other hand, in two other cases antibodies demonstrable in CPT with one hour incubation were present for a relatively short period, and in one case no antibodies could be demonstrated in this test at all, in spité of a good virus multiplication in the alimentary tract.

In 4 out of 5 cases with homologous pre-existing seroimmunity to type 3, only a transient rise of antibodies was demonstrated. In none from these 5 cases did the antibody rise in the more sensitive tests precede the antibody rise in CPT with one hour incubation, even when the absolute levels were lowest without any exception in the CPT with one hour incubation of the virus-serum mixture.

The titers estimated in CPT with 6 hour incubation were on the same level as in the pH test with one or 6 hour incubation, the titers in IIT were in all cases higher than in any test performed with 100 TCD_{50} of virus (Fig. 4).

Even though pH test with 6 hour incubation is more sensitive than pH test with 1 hour incubation, the effect of the duration of incubation of virus-serum mixture is lower than in CPT.

The case 1/HB attracted our special attention. After feeding allowed by a short period of virus excretion antibodies demonstrable in CPT with one hour incubation appeared in the 14th day-sample without any increase of antibody titers demonstrable in the pH tests and the CPT with 6 hour incubation, these tests

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having revealed antibodies already in the pre-immunization sample of serum. In accordance with Sabin's conception these results could be interpreted as a case of transformation from low to high avidity antibodies (1).

In this case, however, a foufold increase of type 3 antibody titer was demonstrated in IIT. For this reason we carried out the following experiment: 4 ml of medium were added to three mixtures, the first of which contained 0.5 ml of virus suspension with $10^{.5}$ TCD_{50} (per 0.1 ml) and 0.5 ml of 1/4 dilution of pre-immunization sample of serum, with the second containing the same amount of virus and 0.5 ml of 1/4 dilution of serum taken on the 14th day, and the third one containing the same amount of virus and 0.5 ml of medium without serum. After 1, 3 and 6 hours of incubation, samples were drawn and the residual virus activity was estimated. The results of 2 repeated tests are given in Table 9.

These results suggest that the presumed qualitative change of antibody character (avidity) in the sera of the case under discussion can be defined as a difference in the quantity of antibodies present in the first and fifth serum specimen. In order to demonstrate this difference in pH test or in CPT with a prolonged incubation of the virus-serum mixture, by means of the serum dilution end point determination method with 100 TCD_{50} of virus, the quantity of virus not inactivated by the later serum had to be at least 10 times lower.

Discussion

In spite of many important new findings gained in the last years (3, 4, 5, 6), the mechanism of virus inactivation by

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specific antibody remains unclear. It seems, however, that Burnet's presumption of complete reversibility of the union between animal virus and specific antibody (7) has to be reconsidered. So, for instance, Gard (3, 4) proves that the virus-antibody reaction proceeds in two steps. In the first step the union is reversible, with the prolonged time of contact a stable complex is formed. For this second step Gard uses the term immunoinactivation.

It is well known that the inactive virus-serum mixture can be rendered infectious by dilution (dilution phenomenon). The higher sensitivity of the pH test is probably due to the low dilution of the virus-serum mixture at the time of its coming into contact with susceptible cells (dilution factor 0.5 in contrast to 5 - 10 in CPT). Other factors, as e.g. a certain delay in the appearance of the cytopathogenic effect due to small quantities of antibodies which enable the cells to produce enough acid metabolits before their destruction by virus action (8), play probably a less important role. One hour incubation with subsequent dilution of the reaction mixture in the routine CPT is completely insufficient to demonstrate small quantities of antibody. The neutralizing effect, if it occurs in the measuring system, inhibiting the development excess in the measuring system, inhibiting the development of virus infection. The virus-antibody union is doubtlessly strengthened by prolongation of the incubation period, and higher titers are obtained, often comparable to those achieved in the pH test.

When considering the problem of "high avidity" and "low avidity" antibodies on the basis of data gained in simultaneous

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investigation of sera in both pH and cP tests, we can summarize our present experience in three following suggestions:

1) we assume that the demonstration of pH antibodies only (in absence of CP antibodies) need not signify the presence of antibodies of different quality, but rather the presence of small amounts of antibodies, which can be demonstrated only by the more sensitive pH test. We have found, for example, a considerable difference in the frequency of pH antibodies only between the group of the youngest infants with predominantly maternal antibodies, and the age group over 20 years. The more detailed analysis performed in the age group of children up to 6 months (see Table 2) shows that in the first period of life the newborns have approximately the same antibody content as the adults over 20 years. In the course of the further months of life the antibody levels rapidly drop,and it seems that on a certain grade of this decrease antibodies are demonstrable only in the pH and no more CP test.

The case 1/HB suggests that the so called change of antibody avidity which occurs according to Sabin as a result of an antigenic stimulus is in fact - at least in some cases - due to the insufficiency of the serum dilution end point method with 100 TCD_{50} of virus to detect in pH test small quantitative changes in antibody levels.

3) On the other hand, the different dynamics of the antibody formation followed up by means of different tests and the considerable differences found in some cases without pre-existing antibodies between the titers estimated in pH tests and the titers in CPT with 1 and 6 hour incubation, and even in IIT, can

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be hardly explained otherwise than by a different and, in the course of infection, changing nature of antibodies.In these cases even the prolonged incubation of the virus-serum mixture in the CPT, recommended by Perkins et all. (9) and by Verlinde et all. (10) was without essentional effect on the antibody titers.

It seems that in persons without homologous immunological experience in the early stages of infection antibodies are produced, which are characterized by a considerable lack of ability to form with viruses complexes resistent to the influence of dilution.

The routine CP test with one hour incubation of virus-serum mixture at room temperature is not a suitable method for estimating the actual state of immunity of an individual or population to polioviruses. This seems to apply especially to type 3. This finding may be in relation to the lower immunologic activity of at least some type 3 strains.

When studying the antibody response in vaccinated persons,the simultaneous use of both pH and CP tests proves to be fully justified. In non-immunes the antibody response is more frequent, earlier and higher in the pH test than in the CP test. These differences are more pronounced when Salk vaccine is administered than in infections with attenuated live viruses. In persons with homologous immunity more frequent and in many cases more significant antibody rises were found in CPT with one hour incubation period in pH test.

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Summary

On the basis of results of serological investigations performed by the conventional CP and pH tests it is recommended to use the pH test for estimating the actual state of seroimmunity to polioviruses. In the pH test antibodies (especially to type 3) are determined even in persons with a very low level of humoral immunity.

For determination of antibody response in vaccinated persons it is suitable to use both pH and CP tests simultaneously. In individuals without homologous antibodies prior to vaccination the antibody response was more frequent in pH test, in persons with pre-existing antibodies more frequent rises were found in CP test.

When studying the antibody response in a group of young adults vaccinated with type 3 attenuated poliovirus, different methods of neutralization tests were used: CP tests with 1 hour incubation of the virus-serum mixture at room temperature and 6 hour incubation at 37°C, the pH tests with 1 hour incubation at room temperature and 6 hour incubation at 37°C, and the immunoinactivation test according to Sven Card.

The results show that in persons without homologous pre-existing seroimmunity earlier and especially in initial phases of antibody development higher antibody rises were demonstrated in pH tests than in CP tests with 1 and 6 hour incubation, in some cases even higher than in immunoinactivation test (IIT). In other cases the titers estimated in IIT were on the same level as those found in the pH tests.

In persons with pre-existing homologous seroimmunity a simultaneous antibody rise was demonstrated by the different tests

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used. The titers in CP test with 6 hour incubation were approximately the same as in pH tests, titers in IIT were higher than in pH tests.

The duration of the incubation of the virus-serum mixture haf a small influence on the antibody titers in pH tests than in CP tests.

On the basis of the results obtained some aspects of the problem of low and high avidity antibodies are discussed.

References

1. Sabin A.B. Spec. Publ. N.Y. Ac. Sci., 5,113, 1957.
2. Zacek et al., Paper presented on the International epid. symp., Prague, 1960.
3. Gard S., Arch. ges. Virusf., VII,449, 1957.
4. Gard S., Ac. Path.Micr. Scand., 37, 21, 1955.
5. Dulbecco R., Vogt M., Strickland A.G.R., Virology,2,162,1956.
6. Kjellen L., Arch.ges. Virusf., VII, 307, 1957.
7. Burnet F.M., Principles of Animal Virology, Acad. Press. New York, 1955, 283, 1955.
8. Youngner J.S., Ann. N.Y. Acad. Sci., 61, 774, 1955.
9. Perkins E.T., Placido Sousa, Tobin J.O.H., Br. Jour.Exp.Path., 39/2,171, 1958.
10. Verlinde J.D., Wilterdink J.B., Kret A., Arch.ges. Virusf., VIII,549,1959.

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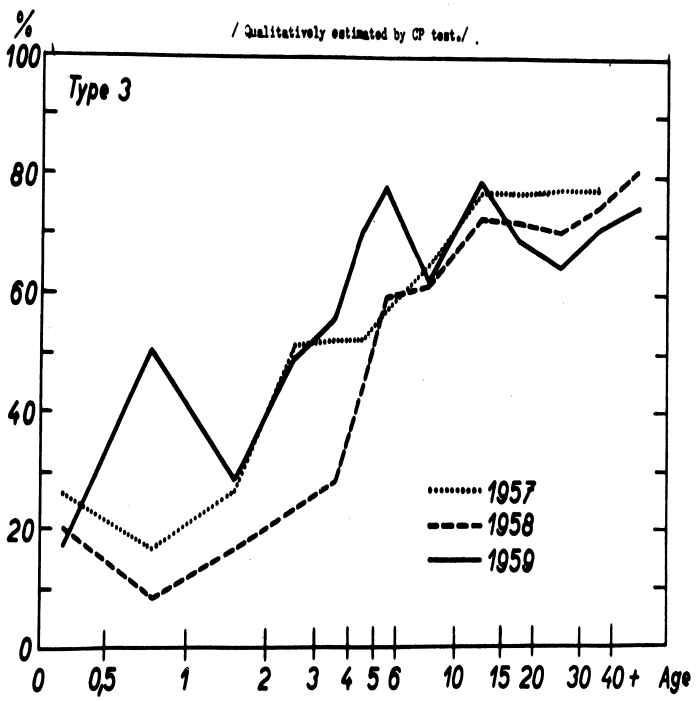
Fig. 3 STATUS OF TYPE 3 ANTIBODY IN GENERAL POPULATION IN ÚSTÍ AND JIHLAVA REGIONS (average value stated for both regions).

/ Qualitatively estimated by CF test./ .



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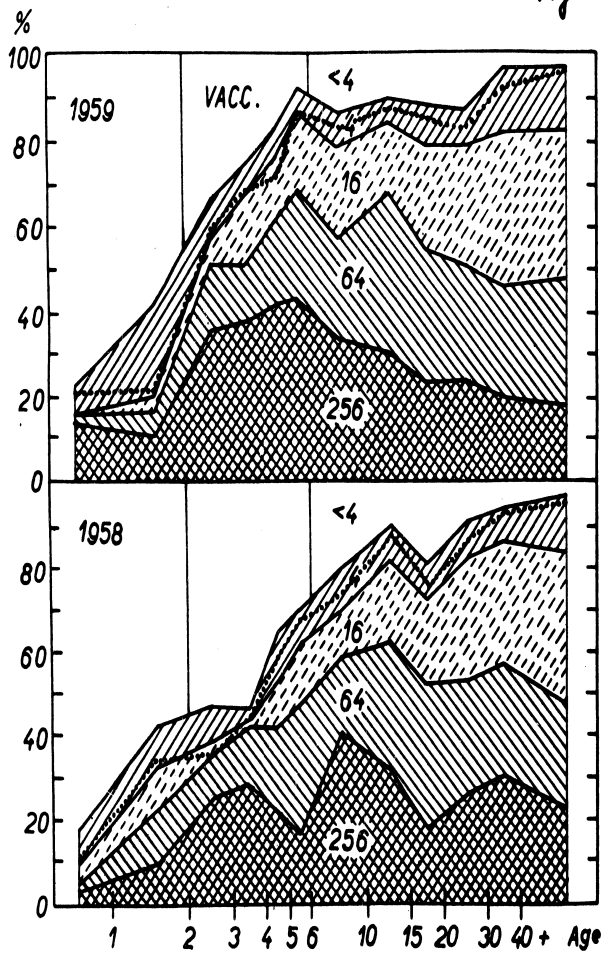
STATUS OF TYPE 1 POLIOMYELITIS ANTIBODY IN GENERAL POPULATION OF ÚSTÍ REGION.

/ Quantitatively measured by NH test./

Fig. N4



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Poliomyelitis Antibodies Estimated in 2 Consecutive Serological Surveys Performed in General Population in 2 Regions

The percentage of Sera in which Antibodies were Demonstrated in Both pH and CP tests, in pH Test only and in CP test only

Year	Age group	Type I				Type 2				Type 3			
	pH	-	+	-	+	-	+	-	+	-	+	-	+
	CPT	-	-	+	+	-	-	+	+	-	-	+	+
1958	0-0.5	52.3	13.7	3.0	31.0	45.5	10.7	2.2	41.6	63.8	15.2	3.2	17.8
	0.5-2	76.2	3.6	-	20.2	47.0	6.0	0.5	46.5	78.2	6.7	-	13.1
	2 - 4	55.2	5.9	1.2	37.7	33.8	9.0	-	57.2	64.9	9.2	1.2	24.7
	4 - 6	36.8	10.7	0.6	51.9	10.0	6.8	1.3	81.9	34.8	13.8	0.7	50.7
	6 -10	16.2	10.4	0.6	72.8	4.5	2.4	0.7	92.4	27.0	11.6	1.3	60.1
	10-15	15.3	6.5	1.2	77.0	8.2	3.6	-	88.2	16.0	8.9	0.6	74.5
	15-20	18.1	7.8	1.2	72.9	11.6	6.6	1.4	80.4	19.6	8.5	0.7	71.2
	20-30	9.6	5.4	0.5	84.5	7.6	4.4	0.6	87.4	18.0	11.0	1.0	70.0
	30-40	9.7	2.7	1.0	86.6	5.5	4.8	0.5	89.2	15.7	9.7	1.1	73.5
	40 +	6.4	3.0	3.1	87.5	5.0	4.7	3.6	86.7	16.0	8.1	5.0	70.9
1959	0-0.5	41.2	15.2	1.6	42.0	35.4	20.0	-	44.6	61.6	21.2	0.8	16.4
	0.5-2	63.0	9.5	0.4	27.1	49.3	14.0	-	36.7	67.2	12.5	-	20.3
	2 - 4	25.6	7.2	0.4	67.2	16.0	12.7	0.6	70.7	34.6	13.0	-	52.4
	4 - 6	10.2	5.3	-	84.5	6.9	6.0	-	87.1	16.0	9.0	-	75.0
	6 -10	17.6	6.0	-	76.4	3.0	6.0	1.0	90.0	25.2	12.5	1.1	61.2
	10-15	11.0	6.7	-	82.3	4.8	2.8	1.1	91.3	14.5	6.0	1.1	78.4
	15-20	12.8	7.0	2.3	77.9	12.8	5.7	1.7	79.8	21.2	9.0	1.2	68.6
	20-30	15.0	4.6	-	80.4	15.5	4.5	-	80.0	17.8	14.2	0.4	67.6
	30-40	4.9	7.2	1.2	86.7	8.6	6.9	-	84.5	17.2		1.2	61.4
	40 +	4.6	6.8	-	88.6	4.2	5.0	0.8	90.0	10.6	14.7	0.4	74.3

Note: These data are based on pH and CPT, performed with 100 TCD_{50} of virus and 1 hour incubation of the virus-serum mixture at room temperature.

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Table 2

Poliomyelitis Antibodies Estimated in 2 Consecutive Serological Surveys Performed in General Population in 2 Regions

The percentage of Sera in which pH antibodies only were Demonstrated from the Total Number of Sera Positive in at Least One Test Used

Age group	Number of sera investigated	Antibodies Present					
		Type 1		Type 2		Type 3	
		Number of sera positive in at least one test used	Percentage of sera with pH antibodies only	Number of sera positive in at least one test used	Percentage of sera with pH antibodies only	Number of sera positive in at least one test used	Percentage of sera with pH antibodies only
0-0.5 y +)	206	103	31.1	125	26.4	76	48.6
0.5-5 y	901	457	14.7	618	14.7	419	54.9
5 - 10 y	534	444	9.1	515	5.2	672	9.7
10 - 20 y	677	568	7.8	612	5.5	569	10.0
20 + y	1214	1115	5.3	1122	5.6	1026	14.1
Total	3532	2687	9.3	2992	8.3	2507	16.1

Note: These data are based on pH and CPE tests, performed with 100 TCD_{50} of virus and 1 hour incubation of the virus-serum mixture at room temperature.

+) y = year.

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Table 3

The Percentage of Sera, in which pH Antibodies only were Demonstrated from the Total Number of Sera Taken from Children Aged Up to 6 Months, which were Positive at Least One Test Used

Aged group	Number of sera investigated	Antibodies Present					
		Type 1		Type 2		Type 3	
		Number of sera positive in at least one test only	Percentage of sera with pH antibodies only	Number of sera with pH positive in at least one test only	Percentage of sera with pH antibodies only	Number of sera with pH positive in at least one test only	Percentage of sera with pH antibodies only
0-1 m +)	26	19	15.8	23	4.3	16	31.1
1-2 m	39	27	18.5	30	13.3	20	35.0
2-3 m	49	23	26.1	36	36.1	22	54.5
3-4 m	28	11	36.2	16	56.2	7	71.4
4-6 m	64	23	61.5	20	30.0	11	72.5
Total	206	103	31.1	125	26.4	76	48.6

Note: These data based on pH and CPE tests, performed with 100 TCD_{50} of virus and one hour incubation of the virus-serum mixture at room temperature.

+) m = month.

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Table 4

Investigation of Paired Serum Specimens Obtained in Children Vaccinated with Three Types of Attenuated Live Polioviruses (Sabin) and/or with the 4th Dose of Salk Vaccine

/1 ml Subcutaneously/

Development of pH and CP Antibodies in Children Without Preexisting Homologous Immunity

Sabin

Type 1 (47 cases)

CP							
1024							1
256					2		
64			1	5	8		3
16			3	10	2		1
4	1	5					
4	1	3	1				
pH	4	4	16	64	256		1024

Type 2 (14 cases)

CP							
1024							1
256							
64				2	1		1
16				3	2		
4				1			
4	2				1		
pH	4	4	16	64	256		1024

CP							
1024							
256				1			
64				2	2		1
16			4	13	1		
4			9	2			
4	2	5	1				
pH	4	4	16	64	256		1024

Salk

Type I (102 cases)

CP							
1024							
256							
64				1	1		
16	1	2		1	1		1
4	4	6		3			
4	41	25	15				
pH	4	4	16	64	256		1024

Type 2 (29 cases)

CP							
1024				3			2
256					1		
64				1	2		
16			1	4			
4		1	5	2			
4	7						
pH	4	4	164	64	256		1024

CP							
1024							2
256							
64				1	3		1
16			1	3	10	5	1
4			5	16	13	2	1
4	13	20	12	4			
pH	4	4	16	64	256		1024

Note: These data are based on pH and cP tests, performed with 100 TCD_{50} of virus and 1 hour incubation of virus-serum mixture at room temperature.

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Table 5

Investigation of Paired Serum Specimens Obtained in Children Vaccinated with Three Types of Attenuated Live Poliovirus (Sabin) and/or with the 4th Dose of Salk Vaccine (1 ml Subcutaneously)

Development of pH and CP Polio Antibodies in Children with a Low Preexisting Homologous Immunity, with Antibodies Demonstrated only in pH test

Sabin

Type 1 (8 cases)

CP	pH = 4x	8x	16x	32x	64x and
1024					
256			1		
64			1		
16	1				
4	1	1			
4	1	1		1	

Type 2 (22 cases)

CP	pH = 4x	8x	16x	32x	64x and
1024					
256					
64		1	1	1	3
16		1	2		
4				1	
4	1				

Type 3 (15 cases)

CP	pH = 4x	8x	16x	32x	64x and
1024					
256					
64	1		1		2
16	1	1	2		
4		1	3	1	
4	1		1		

Salk

Type 1 (19 cases)

CP	pH = 4x	8x	16x	32x	64x and
1024					
256					1
64					
16					2
4	2	1		3	2
4	1	2			
4	1		1		

Type 2 (31 cases)

CP	pH = 4x	8x	16x	32x	64x and
1024					
256			1		6
64					5
16	1	1		3	5
4	1	1	1	1	
4		1		1	
4	1				

Type 3 (42 cases)

CP	pH = 4x	8x	16x	32x	64x and
1024					
256				1	
64			1	1	
16	1	1		1	1
4		2	2	5	1 1
4	1	1	1	4	2 2
4	5	2	2	1	2

Note: These data are based on pH and CP tests, performed with 100 TCD_{50} of virus and 1 hour incubation of virus-serum mixture at room temperature.

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Table 6

Investigation of Paired Serum Specimens Obtained in Children Vaccinated with Three Types of Attenuated Live Polioviruses (Sabin) and/or with the 4Th Dose of Salk Vaccine (1 ml Subcutaneously

Development of pH and CP Antibodies in Children with Solid Preexisting Homologous Immunity (with Antibodies Demonstrable in pH and CP Test)

Sabin

CP	Type 1 (59 cases)					pH
64x and	1				1	64x and
32x						32x
16x	1	3	2			16x
8x	3					8x
4x	9	11	2	3		4x
=	14	6	2	1		=
=	4x	8x	16x	32x	64xand	

CP	Type 2 (78 cases)					pH
64x and	6	1	4			64x and
32x						32x
16x	1	1	6	2	3	16x
8x						8x
4x	8	9	2	3	2	4x
=	23	5	2			=
=	4x	8x	16x	32x	64xand	

CP	Type 3 (56 cases)					pH
64x and				2	64xand	64x and
32x						32x
16x	2	4	3	3	2	16x
8x		1				8x
4x	7	7	1			4x
=	20	3		1		=
	4x	8x	16x	32x	64xand	

Salk

CP	Type 1 (152 cases)					pH
64x and	1	1	2	4	1 3	64x and
32x				1		32x
16x	4	6		7	2 2	16x
8x	2					8x
4x	16	28	2	6	1 2	4x
=	49	9	1	3		=
=	4x	8x	16x	32x	64xand	

CP	Type 2 (213 cases)					pH
	2	1	8	2	29	
32x						32x
16x	9	11	3	19	6 9	16x
8x						8x
4x	15	22	6	4	1 3	4x
=	47	13	1			=
=	4x	8x	16x	32x	64xand	

CP	Type 3 (119 cases)					pH
	1			3	1 4	
32x	1		1			32x
16x	5	11	1	7	1	16x
8x						8x
4x	20	15	1	2	1	4x
=	33	9	1	1		=
=	4x	8x	16x	64xand		

Note: These data are based on pH and CP tests, performed with 100 TCD_{50} of virus and 1 hour incubation of virus-serum mixture at room temperature.

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Table 7

Investigation of Paired Serum Specimens Obtained in Children Vaccinated with Three Types of Attenuated Polioviruses (Sabin) and with the Fourth Dose of Salk Vaccine (1 ml Subcut.)

Development of pH and CP Antibodies in relation to the Preexisting Homologous Immunity

	Sabin						Salk					
Type	Preexisting state of seroimmunity		Number of persons investigated	Positive serological response in per cent			Preexisting state of seroimmunity		Number of persons investigated	Positive serological response in per cent		
	pH	CP		pH	CP	pH and/or CP	pH	CP		pH	CP	pH and/or CP
1	-	-	47	98	89.4	98.0	-	-	102	59.8	20.6	59.8
	+	-	8	87.5	62.4	87.5	+	-	19	84.4	89.5	94.7
	+	+	59	55.9	61.0	76.2	+	+	152	52.7	59.3	67.2
2	-	-	14	89.5	78.5	85.9	-	-	29	75.9	75.9	75.9
	+	-	22	95.6	95.6	95.6	+	-	31	90.4	96.8	96.8
	+	+	78	59.0	61.5	70.5	+	+	213	65.9	70.3	76.6
3	-	-	43	95.5	81.4	95.5	-	-	112	88.5	55.1	88.5
	+	-	15	93.8	86.6	93.8	+	-	42	83.2	71.5	88.0
	+	+	56	48.1	57.2	64.2	+	+	119	50.4	63.0	72.0

Note: These data are based on pH and CP tests, performed with 100 TCD_{50} of virus and one hour incubation of the virus-serum mixture at room temperature.

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Table 8

Type 3 Antibody Response Determined by Different Methods of Neutralization Tests in the Case 1/HB, Fed with 100,000 TCD_{50} of Type 3 Attenuated Live Poliovirus

Day of sampling	0	4	7	10	14	21	28	35	42	84
Virus excretion	-	-	+	+	-	-	-	-	-	-
Neutralization test										
CP-test with 1 hour incubation	0	0	0	0	8	3	5	8	3	5
CP-test with 6 hours incubation	32	20	20	20	32	51	32	32	32	16
pH test with 1 hour incubation	32	8	8	16	16	16	32	16	16	8
pH test with 6 hours incubation	32	16	16	32	32	32	32	16	16	8
11T	31	48	32	48	140	140	140	95	41	48

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Table 9

Residual Virus Activity in Samples Drawn in Different Time Periods from Virus-Serum Mixtures, Containing Serum Taken Before Type 3 Virus Was Fed (S-1/ and Serum Taken on the 4th Day After Feeding (S-1

Incubation of the virus-serum mixture	1st Experiment			2nd Experiment		
	Virus control	S - 1	S - 5	Virus control	S - 1	S - 5
1 hour	3.8	3.6	3.8	3.3	3	3.1
3 hours	3.9	3.1	2.8	ND	ND	ND
6 hours	3.7	2.8	2.0	3.4	2.8	1.7

Note: The samples were immediately after drawing diluted in ten-fold steps and then tissue culture tubes were inoculated from each dilution.

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ACADEMY OF MEDICAL SCIENCES OF THE USSR

INSTITUTE FOR POLIOMYELITIS RESEARCH

STAT

THE STUDY OF CONDITIONS SECURING OPTIMAL VIRUS YIELDS IN PRODUCTION OF LIVE POLIOVIRUS VACCINE PREPARED FROM A.SABIN ATTENUATED STRAINS

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Large-scale serial production of live poliovirus vaccine from the Sabin's strains was first organized in the USSR in 1958-1959 (1) at the AMS USSR Institute for poliomyelitis research (2) and this made it possible to start during 1959 with mass immunization of the population (3,4).

The object of the present work was to study the influence exercised on the virus yield by the following factors:
1) the amount of virus employed to inoculate the culture, 2) the number of cells in 1 matrass, 3) the amount of medium in 1 matrass used for inoculation, 4) horizonal swinging of inoculated cultures, 5) procedure adopted to obtain distilled water for preparation of the medium employed to get the cultures and to grow the virus, 6) method used in preparing the medium, 7) filtration.

Materials and Procedures.

Cultures. Monkey kidneys were trypsinized at 4°C or at 37°C by a method employed in the laboratory for tissue culture of the AMS USSSR Institute for poliomyelitis research. Matrasses made of neutral glass were being filled with cells at the rate of 100 000 cells in 1 ml. of the medium per 1 cm^2 of the matrass bottom area. As a medium for the growth of cells was used a 0.5% solution of enzymatic hydrolysate of lactalbumin in Hanks saline with 2% calf serum, pH of the medium being 7.0-7.1. The medium was changed on the 5-6th day with the pH at the time of change equalling 7.3-7.5. The culture was inoculated with the virus on the 8-9th day following inoculation, in presence of a compact cellular monostratum.

-Virus.

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Virus. To inoculate the culture A.Sabin's attenuated strains were used of the type I - LSc,2ab, of the type II- P 712,ch,2ab, of the type 3 -Leon 12 ab, all of which were run through 1 passage in the tissue culture of a monkey kidney. The virus was grown at 33.5-34°C. The collection of the virus was effected at 3+ or 4+ of degeneration, with samples thereof stored at -20°C, prior to titration.

Cell count. The cells were taken from a matrass with the aid of a 0.2% dinatrium=ethylene=diamine-tetracetate/versen/ solution on a phosphate buffer without magnesium chloride and calcium chloride. Cell count in each batch was effected by 3 laboratorians simulataneously, whereby each one of them counted the number of squares in the hemocytometer,containing each 600-800 cells. To arrive at the final estimation mean arithmetic value was calculated for the cell concentration in 1 ml.

Swinging of the matrasses. - This was effected on a laboratory apparatus at a rate of 28 swings per 1 minute, with the lateral amplitude of 15° in both directions from the horizontal, continuously, until completion of cell degeneration and virus collection.

Inoculation medium. The 0.5% enzymatic hydrolyzate of lactalbumin solution prepared on the Earl's solution with 540 mg% sodium bicarbonate and 400 mg% glucose was prepared after Melnick's (5) and Sabin's (6) formula with the pH of the medium brought up to 7.5 by passing gaseous CO_2 through it. In a series of experiments a medium consisting of 0.5% lactalbumin hydrolyzate and 800 mg% sodium bicarbonate and 400 mg% glucose, was used, this being prepared by dissolution of dry ingredients in distilled water with subsequent

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filtration through the ST-1 asbestos filre. pH of this medium was brought up to 7.5 by passing gaseous CO_2 through it. Usually the medium was being prepared on water, subject to a triple destillation in distillation apparatuses; several trial batches of the medium were prepared by using water preliminarily distilled and demineralized in a ion-exchange column with cationites and anionites, in a vessel coated with silicic enamel.

Virus filtration. The virus, collected from inoculated matrasses after cell degeneration, upon single freezing and defreezing, was run through a plate separator of the ASG type with 11000 revolutions per minute and at a rate of 25-30 litres per hour and then was passed through asbestos filtres "S" (diameter of pores= 0.5 microns), these latter having been preliminarily saturated with 0.5 ml of a 10% gelatin solution. During filtration the pressure did not exceed 0.8 ata. A total of 50 to 100 litres of the virus were run through 1 dcm^2 of the plate area. Virus samples were being collected in the course of filtration, so as to determine the virus adsorption characteristics on the filters. Sample batches were kept at $-20^{0}C$, untill titration time.

Titration of the virus. The titre of the virus expressed in plate-forming units (PFU) was determined after Dulbecco (7) procedure , modified by Hsiung and Melnick(8), for which purpose a 0.8% or 1% cover-glass agar with 440 mg% of sodium bicarbonate and 2% calf serum was used. Cultures covered with agar, following their inoculation , were incubated at $34^{0}C$. Titres are expressed as PFU numbers per 1 ml. of the virus.

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RESULTS

1. The Significance of the Virus Count for Inoculation.

In these experiments various amounts of the virus of the I type were put in 1.5 litre matrasses with the surface area of 300 sm^2, into which, prior to this, 300 or 350 ml of the medium for virus cultivation had been introduced. To prepare one dose of the virus 10 matrasses were taken. The results of 2 experiments are listed in tables No 1 and No 2.

As seen from the figures included in these tables inoculation of the culture with the virus doses inferior to 10^3-10^4 of PFU in our experiments resulted in a reduced virus yield.

2. The Significance of the Cell Count in the Culture.

In this experiment the same amount of the virus was used to inoculate 2 groups of matrasses (1.5 litres). One of them comprised 10 matrasses with very good growth index (40.8 mln.cells in 1 matrass) and another 10 matrasses with low growth index (9.8 mln.cells in 1 matrass). In both groups the monostratum was complete. In the matrasses with good growth the titre of the virus obtained was 11.2 x 10^6 PFU/ml (3360 x 10^6 PFU from 1 matrass), while in those with the low growth index the titre was 2.7 x 10^6 PFU (810 x 10^6 PFU from 1 matrass). Thus, the amount of the virus actually obtained proved to be proportional to the cell count in the culture.

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T a b l e 1.

Relationship between the Inoculating Dose of the Virus and its Actual Yield.

Virus of the I type, Sabin's strain. Matrass capacity - 1.5 l, botton area -300 cm^2, cells grown in 1 matrass - 40.8 mln, the amount of medium in each matrass- 300 ml.

Virus inoculation dose in PFU :	$3.5x10^5$	$3.5x10^4$	$3.5x10^3$	$3.5x10^2$
The titre of the virus obtained in PFU per 1 ml (x 10^6)	10.7	11.5	11.2	2.75
The amount of the virus in PFU obtained from 1 matrass (x 10^6)	3225	3450	3360	825

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T a b l e 2.

Relationship between the Inoculating Dose of the Virus and its Actual Yield.

Virus of the I type, Sabin's sttain. Matrass capacity - 1.5 litres, bottom area- 300 cm^2, the amount of medium in each matrass - 350 ml.

Virus inoculation dose in PFU	6.7×10^7	6.7×10^6	6.7×10^5	6.7×10^4	6.7×10^3	6.7×10^2	6.7×10^1
The titre of the virus obtained in PFU per 1 ml (10^6)	16	16.5	17.2	12.8	8.2	4.7	3.5
The virus yield in PFU per 1 matrass ($\times 10^6$)	5600	5800	6000	4500	2900	1650	1200

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3. The Significance of the Matrasses' Swinging After Inoculation.

These experiments with differing amount of the medium per 1 matrass were carried out on several occasions. Some of the results obtained are included in tables NoNo 3,,4 and 5. During the process of swinging no acceleration of cytopathogenic action of the virus could be observed.

As seen from the data relative to the virus yield in the cited experiments, the swinging of matrasses following inoculation tends to increase the virus yield by 1.3-2.2 times.

4. The Significance of the amount of the Medium Taken for Inoculation.

Tables 3 and 4 include data on the virus yield from inoculated matrasses containing 50 and 200 ml of the medium and subjected to swinging upon their inoculation. Table 6 is illustrative of the virus yield from stationary matrasses, whereto, prior to inoculation there were introduced 100 or 300 ml of the medium. From the data listed in these tables one can see that the virus yield from the matrasses containing about 10 ml of the medium per 1 milln. of cells was 1.4-2 times higher than in those containing 2-2.5 ml of the medium per 1 milln. of cells.

5. The Importance of the Quality of Distilled Water for the Preparation of the Media and for the Procedure to be Used for this Purpose.

The obtaining of large quantities of water, now used for the preparation of the media, which provides its triple distillation in glass apparatuses, presents considerable difficulties.

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We have, therefore, suggested to use for the preparation of medium employed in growing tissue cultures and in obtaining the virus- water demineralized by passing it through a ion-exchange column, or that dimineralized and then subjected to a single distillation in a metal reactor, coated with silicic enamel. By its electro-conductivity such water is in no way inferior to that triply distilled in glass apparatuses. The media, prepared on water drawn from both sources, were compared with respect to their suitability for the growing of tissue cultures (table 7), for the sensitivity of cultures, grown on these media, to the poliovirus (table 8) and for the suitability of th the media in the virus cultivation (table 9).

The data cited here show that the prodedure employed to obtain distilled water for the preparation of the media, apparently, does not influence, substantially, the rate and quality of the cultural growth, as well as fails to affect the sensitivity of the cultures to the poliovirus or diminish its yield. The only exception form media for the culture growing prepared on the water demineralized in ion-exchenge columns. When inoculating small amounts of trypsinized cells into these media the results are inferior to those obtained with with media prepared on water drawn from the other sources. This fact has been repeatedly confirmed in a series of experiments performed on a large number of cultures.

The method now used for the preparation of a medium for the virus cultivation is rather laboricus. We have tested a medium with a 0.5% solution of lactalbumin hydrolyzate, prepared by dissolution of dry ingredients in distilled water with subsequnet filtration.

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T a b l e 3.

The Significance of the Matrasses' Swinging and of the Volume of the Medium in a Matrass for the Virus Yield.

Experiment No 1. Sabin's stmain of the I type , inoculation with $4x10^6$ PFU in each matrass, matrass' capacity-1 l., area-170 cm^2, cell count in 1 matrass -$26.6x10^6$. Swinging at the rate of 28 per minute, continuously untill complete cell degeneration. 16 matrasses per experimental variant.

Experimental variant	Titre in PFU of the virus obtained ($x10^6$) in 1 ml.	Amount of the virus from 1 matrass in PFU($x10^6$)	Relative virus yield Variant-B=$	Virus yield per 1 cell in PFU
A. 50 ml of the medium in 1 matrass, with swinging	41	2050	137%	77
B. 200 ml of medium per 1 matrass, with swinging	16.5	3300	220%	124
C. 200 ml of medium per 1 matrass, stanionary	7.5	1500	100%	57

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T a b l e 4.

The Significance of the Matrasse' Swinging and of the Volume of the Medium in a Matrass for the Virus Yield.

Experiment No 2. Sabin's strain of the I type, inoculation with $4x10^5$ PFU in each matrass, matrass capacity- 1 l., area 170 cm^2, cell s in the matrasses -not counted. Swinging at a rate of of 28 per minute, continuously, unitill complete degeneration of cells. 16 matrasses per each experimental variant.

Experimental variant	Titre in PFU of the virus obtained ($x10^6$) in 1 ml	Amount of the virus from 1 matrass in PFU ($x10^6$)	Relative virus yield. Variant C= = 100 %
A. 50 ml of the medium in 1 matrass, with swinging	43	2150	66%
B. 200 ml of the medium per 1 matrass, with swinging	21.6	4320	132%
C. 200 ml of the medium per 1 matrass, stationary	16.4	3280	100%

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T a b l e 5.

The Significance of the Matrasses' Swinging for the Virus Yield.

Experiment No 3. Sabin's strain of the I type, inoculation with 1.3×10^4 PFU in each matrass, matrass capacity-1.5 l., area-300 cm^2, cell count per 1 matrass 41×10^6. Swinging at a rate of 28 per minute, continuously, untill complete cell degeneration. 10 matrasses per each experimental variant.

Experimental variant	Titre in PFU ($\times 10^6$) obtained in 1 ml	Amount of the virus from 1 matrass in PFU ($\times 10^6$)	Relative virus yield Variant B= 100%	Virus yield per 1 cell in PFU
A. 100 ml of the medium in 1 matrass, with swinging	32	3200	130%	79%
B. 100 ml of the medium in 1 matrass, stationary	25	2500	100%	61

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T a b l e 6.

The Significance of the Amount of the Inoculation Medium for the Virus Yield.

Savin's strain of the I type, inoculation with 1.3×10^4 PFU in each matrass, matrass capacity- 1.5 l., area- 300 cm^2, cell count in 1 matrass- 30.8×10^6. Stationary cultures.

Experimental variant	Titre in PFU: The virus of the yield from virus obatained in 1 ml	The virus yield from 1 matrass in PFU ($\times 10^6$)	Relative virus yield Variant A= 100%	Virus yield per 1 cell in PFU
A. 300 ml of the medium in 1 matrass	11.2	3360	100%	82
B. 100 ml of the medium in 1 matrass	25.0	2500	75%	61

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Table 7

Suitability of the Media Prepared with Different Types of Water for Cultivation of the Monkey's Renal Cells

10 matrasses per 1 experimental variant. Medium changed on the 4-6th day. Cells counted on the 7th day.

Number of cells per 1 cm^2 of the matrass bottom area	The type of water used for the preparation of the medium	Number of cells cultivated per 1 cm^2 in 7 days ($x10^3$) ± mean square deviation
62000	A. Demineralized in a ion-exchange column.	131 ± 11.6
	B. Demineralized and distilled in a reactor with enamel coating	292 ± 17.5
	C. Triply distilled in a glass apparatus	259 ± 20.0
124000	A. Demineralized in a ion-exchange column	294 ± 20.2
	B. Demineralized and distilled in a reactor with enamel coating	324 ± 24.0
	C. Triply distilled in a glass apparatus	298 ± 36.0

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T a b l e 8.

Sensibility to the Poliovirus of Cultures Grown on the Media Prepared with Different Types of Distilled Water.

From bottles containing the preparation cultivated on media with different types of distilled and demineralised water subject to titration was the virus of the I type of the Sabin's strain. Each of 5 bottles cultivated on different media received 0.2 ml of the virus diluted to 10^{-5}.

The type of water used in the preparation of the medium for the growth of the culture	Number of plates in individual bottles	Titre in PFU ($x10^6$) in 1 ml.
A. Demineralised in a ion-exchange column.	33,34, 28, 28	15.2
B. Demineralised and distilled in a reactor with enamel coating	28, 34, 29, 37, 24	15.7
C. Triply distilled in glass apparatuses.	27, 22, 26, 26, 35	13.6

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T a b l e y.

Suitability of Media Prepared with Distilled Water of Differ[illegible] Types for Cultivation of Poliovirus.

Virus of the I type, Sabin's strain. Capacity of the matrasses- 1 l., square area 200 cm^2, inoculated with $5x10^7$ PFU each. Virus introduced diluted in the medium. Cultures are grown in water triply distilled in glass apparatuses. 50-80 matrasses per each experimental variant.

Type of water used in preparing the medium for inoculation of the culture	Titre of the virus obtained in PFU (x 10^6) in 1 ml.
Experiment No 1. Demineralized and distilled in a reactor with an enamel coating . . .	15.0
Triply distilled in a glass apparatus . . .	14.1
Experiment No 2. Demineralized and distilled in a reactor with an enameled coating . .	38.0
Triply distilled in a glass apparatus . . .	40.0

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The amount of sodium carbonate in this variant was equal to 800 mg%, as against 440 mg% in the medium prepared according to the ordinary formula. Results consequent upon cultivation of the virus on the media prepared according to the ordinary and modified procedures are presented in table 10.

Table 10.

Virus Yield with the Media for its Cultivation Prepared According to the Ordinary and Modified Prodedures.

Virus of the I type, Sabin's strain. Matrasses inoculated with 5×10^7 PFU each. Virus introduced in a diluted medium. Matrass capacity-1 litre, square area-200 cm^2, with 50 per each esperimental variant. Cultures gown on a medium prepared with water triply distilled in glass apparatuses.

Type of the medium	Titre of the virus obtained in PFU ($\times 10^6$) in 1 ml.
Medium prepared according to ordinary procendure	18
Medium prepared by dissociation of dry ingredients in 800 mg% of $NaHCO_3$ and 400 mg% of glucose	19

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As seen from the table the virus cultivated on both media had the same titre and this testifies to the suitability of the medium prepared according to the modified procedure for obtaining the virus.

7. The Improtance of Filtration.

Experience gained in production of inactivated poliovirus vaccine clearly shows how great is the importance of properly selected optimal regime of filtration (the selection of a proper charge of the liquid to be filtered in litres per unit of the filter surface, treatment of the filter before operation with substances possessing surface activity , of the type of the beef=peptone bouillon or gelatine). During filtration through sterilizing plates with pores of maximal size of the type № S№ it has been established that the filtrate titre approaches that of the initial virus only after passing 1.5-2 litres of the virus through 1 dcm^2 of the plate area. Preliminary saturation of the filter with a weak gelatin solution (0.5 ml of a 10% solution per 1 dcm^2 of plate surface) tends to considerably reduce the adsorption capacity of the filter.

In this work study was made of adsorption curves for the attenuated poliovirus with asbestos=celluloid filters of the "S" type. Before filtration the virus was freed from suspended particles by passing it through an ASG plate separator. The filter was autoclaved when still moist and before the filtration was saturated with 0.5 ml of a 10% gelatin solution, dissolved in 5 litres of Hanks solution. The virus sample was collected after having run through the filter of 0.5-1-2-3-4-5-10-15-20--30-40-50-70 litres of virus. Adsorption curves are shown on figures No 1 and No 2.

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As seen from these curves the amount of the virus in the first two litres of the filtrate was lower as compared with its quantity prior to filtration. Beginning with the 3d litre the titre of the virus approached the titre of the initial virus. No further fluctuations in the titre could be observed. Thus, the employed filtration procedure proved to be quite acceptable. The titres of the production series of live vaccine before and after filtration are indicated in Table 11.

This table shows that when passing 50-80 litres of the virus through a filter having a diameter of 140 mm and preliminarily treated with 0.5 ml of a 10% gelatin solution, no perceptible reduction in the vaccine titre can be noted. Insignificant flucatuations of the titre in both direction before and after filtration do not go beyond the limits of accuracy in titration.

BRIEF CONTENTS.

Under study were optimal conditions of virus cultivation in production of live poliovirus vaccine from Sabin's strains. The virus yield proves to be uniform with the inoculation of cultures with large doses of the virus; it tends, however, to decline, when the amount of the virus used for inoculation of the culture is below 10000 PFU of the virus. The virus yield is directly proportional to the cell count in the culture. In our experiments the swinging of the matrasses increases the virus yield 1.3-2.2-fold. Introduction of 10ml of the medium per 1 mln. of cells at the time of inoculation raises the virus yield by 1.4-2 times as compared with the introduction of 2-2.5 ml.of the medium per 1 mln. of cells. To grow the culture and obtain the virus fully suitable is the medium prepared with water obtained through distillation of demineralized

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Table 11.

TITRES OF LIVE ATTENUATED POLIOVIRUS / SABIN'S STRAINS/ BEFORE AND AFTER FILTRATION THROUGH ASBESTOS "S" TYPE FILTERS WITH 140 DIAMETER, SATURATED PRIOR TO FILTRATION WITH 0.5 ml OF A 10% GELATIN SOLUTION

Virus type	No. of the series	Virus titre in PFU in 1 ml ($x10^6$), before filtration	Virus titre in PFU in 1 ml.($x10^6$) after filtration
Type I	22	13.2	7.4
	23	9.0	9.0
	24	9.2	8.9
	25	11.5	9.0
	38	3.7	3.3
	41	8.8	10.0
	42	10.0	8.4
	43	19.0	16.4
Type II	31	10.0	7.1
	33	5.5	6.4
	36	13.0	14.7
	37	19.0	12.0
	40	17.7	12.5
Type III	26	11.5	9.0
	27	18.5	13.8
	28	11.0	11.5
	29	18.0	17.3
	39	16.5	18.2
	49	13.4	14.8
	50	11.3	14.3
	51	13.3	13.7

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raw water in a metal reactor with silicic enamel coating. The results obtained with media prepared by dissolution of dry ingredients in distilled water with subsequnet diltration are in no way inferior to those obtained on a standard medium. No perceptible loss of the virus is marked follwoing filtration of 50-80 litres of attenuated Sabin's virus via an asbestos"S" type filter, with 140 mm diameter, and preliminarily saturated with 0.5 ml. of a 10% gelatin solution.

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Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

BIBLIOGRAPHY.

1. Sabin, A.B. J.Am.Med.Ass.,1956,162:1581;
   J.Am.Med.Ass.,1957,164:1216; Brit.Med.J.,1959,1:663.

2. Chumakov,M.P.,Gagrina,L.V.,Lashkevich,V.A.,Dzagurov,S.G.,
   Ralf,N.M.,Fleer,G.P., Voroshilova,M.K.,Robinson,I.A.
   Problems of Virology,1959,5,529.

3. Chumakov M.P., Voroshilova,M.K.,Vasilieva, Bakina,M.N.,
   Dobrova,I.N.,Drozdov,S.G., Podsedlovsky,T.S.,Kostina,K.A.,
   Shirman,G.A., Ashmarina,E.E., Yankevich,O.D.,Uspensky, Yu.S.
   Problems of Virology, 1959,5,529.

4. Chumakov,M.P. and collaborators. On Mass Peroroal Immunization
   of the Population in the Soviet Union with live
   Poliovirus Vaccine from Sabin's strains. Report 2,
   published by the AMS USSR Institute for Poliomye-
   litis Research,1960,77 p.

5. Melnick J.L.Ann.N.I.Acad.Sci.,1955,61,4,p.754-733
   " Bull. Wed.H.O., 1956,14,1,p.129-146.

6. Instructions for Preparation and Control of live vaccine from
   Attenuated Poliovirus Strains. Manuscript, 1959.

7. Dubecco R.Proc.Nat.Acad.Sci.,1952,38,8,747-752.
   J.Exp.Med. 1954,99,2,p.167-182.

8. Hsiung G.D.,Melnick J.L.J.Immunol.,1957,78,p.128.
   Virology 1955,1,p.533.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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T a b l e 4.

The Significance of the Matrasse' Swinging and of the Volume of the Medium in a Matrass for the Virus Yield.

Experiment No 2. Sabin's strain of the I type, inoculation with $4x10^6$ PFU in each matrass, matrass capacity- 1 l., area 170 cm^2, cell s in the matrasses -not counted. Swinging at a rate of of 28 per minute, continuously, unitill complete degeneration of cells. 16 matrasses per each experimental variant.

Experimental variant	Titre in PFU of the virus obtained ($x10^6$) in 1 ml	Amount of the virus from 1 matrass in PFU ($x10^6$)	Relative virus yield. Variant C= = 100 %
A. 50 ml of the medium in 1 matrass, with swinging	43	2150	66%
B. 200 ml of the medium per 1 matrass, with swinging	21.6	4320	132%
C. 200 ml of the medium per 1 matrass, stationary	16.4	3280	100%

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T a b l e 5.

The Significance of the Matrasses' Swinging for the Virus Yield.

Experiment No 3. Sabin's strain of the I type, inoculation with 1.3×10^4 PFU in each matrass, matrass capacity-1.5 l., area-300 cm^2, cell count per 1 matrass 41×10^6. Swinging at a rate of 28 per minute, continuously, untill complete cell degeneration. 10 matrasses per each experimental variant.

Experimental variant	Titre in PFU ($\times 10^6$) of the virus obtained in 1 ml	Amount of the virus from 1 matrass in PFU ($\times 10^6$)	Relative virus yield Variant B= 100%	Virus yield per 1 cell in PFU
A. 100 ml of the medium in 1 matrass, with swinging	32	3200	130%	79%
B. 100 ml of the medium in 1 matrass, stetionary	25	2500	100%	61

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T a b l e 6.

The Significance of the Amount of the Inoculation Medium for the Virus Yield.

Savin's strain of the I type, inoculation with 1.3×10^4 PFU in each matrass, matrass capacity- 1.5 l., area- 300 cm^2, cell count in 1 matrass- 40.8×10^6. Stationary cultures.

Experimental variant	Titre in PFU: (x10^6) of the yield from virus obatai: ned in 1 ml	The virus yield from 1 matrass in PFU (x10^6)	Relative virus yield Variant A= 100%	Virus yield per 1 cell in PFU
A. 300 ml of the medium in 1 matrass	11.2	3360	100%	82
B. 100 ml of the medium in 1 matrass	25.0	2500	75%	61

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Table 7

Suitability of the Media Prepared with different Types of Water for Cultivation of the Monkey's Renal Cells

10 matrasses per 1 experimental variant. Medium changed on the 4-6th day. Cells counted on the 7th day.

Number of cells per 1 cm^2 of the matrass bottom area	The type of water used for the preparation of the medium	Number of cells cultivated per 1 cm^2 in 7 days ($x10^3$) ± mean square deviation
62000	A. Demineralized in a ion-exchange column.	131 ± 11.6
	B. Demineralized and distilled in a reactor with enamel coating	292 ± 17.5
	C. Triply distilled in a glass apparatus	259 ± 20.0
124000	A. Demineralized in a ion-exchange column	294 ± 20.2
	B. Demineralized and distilled in a reactor with enamel coating	324 ± 24.0
	C. Triply distilled in a glass apparatus	298 ± 36.0

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T a b l e 8.

Sensibility to the Poliovirus of Cultures Grown on the Media Prepared with Different Types of Distilled Water.

From bottles containing the preparation cultivated on media with different types of distilled and demineralized water subject to titration was the virus of the I type of the Sabin's strain. Each of 5 bottles cultivated on different media received 0.2 ml of the virus diluted to 10^{-5}.

The type of water used in the preparation of the medium for the growth of the culture	Number of plates in individual bottles	Titre in PFU ($\times 10^6$) in 1 ml.
A. Demineralized in a ino-exchange column.	33,34, 28, 28	15.2
B. Demineralized and distilled in a reactor with enamel coating	28, 39, 29, 37, 24	15.7
C. Triply distilled in glass apparatuses.	27, 22, 26, 26, 35	13.6

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T a b l e 9.

Suitability of Media Prepared with Distilled Water of Differ

Types for Cultivation of Poliovirus.

Virus of the I type, Sabin's strain. Capacity of the matrasses- 1 l., square area 200 cm^2, inoculated with $5x10^7$ PFU each. Virus introduced diluted in the medium. Cultures are grown in water triply distilled in glass apparatuses. 50-80 matrasses per each experimental variant.

Type of water used in preparing the medium for inoculation of the culture	Titre of the virus obtained in PFU (x 10^6) in 1 ml.
Experiment No 1. Demineralized and distilled in a reactor with an enamel coating . . .	15.0
Triply distilled in a glass apparatus . . .	14.1
Experiment No 2. Demineralized and distilled in a reactor with an enameled coating . .	38.0
Triply distilled in a glass apparatus . . .	40.0

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The amount of sodium carbonate in this variant was equal to 800 mg%, as against 440 mg% in the medium prepared according to the ordinary formula. Results consequent upon cultivation of the virus on the media prepared according to the ordinary and modified procedures are presented in table 10.

Table 10.

Virus yield with the Media for its Cultivation Prepared According to the Ordinary and Modified Prodedures.

Virus of the I type, Sabin's strain. Matrasses inoculated with 5×10^7 PFU each. Virus introduced in a diluted medium. Matrass capacity-1 litre, square area-200 cm^2, with 50 per each esperimental variant. Cultures gown on a medium prepared with water triply distilled in glass apparatuses.

Type of the medium	Titre of the virus obtained in PFU ($\times 10^6$) in 1 ml.
Medium prepared according to ordinary procendure	18
Medium prepared by dissociation of dry ingredients in 800 mg% of $NaHCO_3$ and 400 mg% og glucose	19

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As seen from the table the virus cultivated on both media had the same titre and this testifies to the suitability of the medium prepared according to the modified procedure for obtaining the virus.

7. The Improtance of Filtration.

Experience gained in production of inactivated poliovirus vaccine clearly shows how great is the importance of properly selected optimal regime of filtration (the selection of a proper charge of the liquid to be filtered in litres per unit of the filter surface, treatment of the filter before operation with substances possessing surface activity , of the type of the beef=peptone bouillon or gelatine). During filtration through sterilizing plates with pores of maximal size of the type "S" it has been established that the filtrate titre approaches that of the initial virus only after having passed 1.5-2 litres of the virus through 1 dcm^2 of the plate area. Preliminary saturation of the filter with a weak gelatin solution (0.5 ml of a 10% solution per 1 dcm^2 of plate surface) tends to considerably reduce the adsorption capacity of the filter.

In this work study was made of adsorption curves for the attenuated poliovirus with asbestos=celluloid filters of the "S" type. Before filtration the virus was freed from suspended particles by passing it through an ASG plate separator. The filter was autoclaved when still moist and before the filtration was saturated with 0.5 ml of a 10% gelatin solution, dissolved in 5 litres of Hanks solution. The virus sample was collected after having run through the filter of 0.5-1-2-3-4-5-10-15-20--30-40-50-70 litres of virus. Adsorption curves are shown on figures No 1 and No 2.

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As seen from these curves the amount of the virus in the first two litres of the filtrate was lower as compared with its quantity prior to filtration. Beginning with the 3d litre the titre of the virus approached the titre of the initial virus. No further fluctuations in the titre could be observed. Thus, the employed filtration procedure proved to be quite acceptable. The titres of the production series of live vaccine before and after filtration are indicated in Table 11.

This table shows that when passing 50-80 litres of the virus through a filter having a diameter of 140 mm and preliminarily treated with 0.5 ml of a 10% gelatin solution, no perceptible reduction in the vaccine titre can be noted. Insignificant flucatuations of the titre in both direction before and after filtration do not go beyond the limits of accuracy in titration.

BRIEF CONTENTS.

Under study were optimal conditions of virus cultivation in production of live poliovirus vaccine from Sabin's strains. The virus yield proves to be uniform with the inoculation of cultures with large doses of the virus; it tends, however, to decline, when the amount of the virus used for inoculation of the culture is below 10000 PFU of the virus. The virus yield is directly proportional to the cell count in the culture. In our experiments the swinging of the matrasses increases the virus yield 1.3-2.2-fold. Introduction of 10ml of the medium per 1 mln. of cells at the time of inoculation raises the virus yield by 1.4-2 times as compared with the introduction of 2-2.5 ml.of the medium per 1 mln. of cells. To grow the culture and obtain the virus fully suitable is the medium prepared with water obtained through distillation of demineralized

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T a b l e 11.

TITRES OF LIVE ATTENUATED POLIOVIRUS / SABIN'S STRAINS/ BEFORE AND AFTER FILTRATION THROUGH ASBESTOS "S" TYPE FILTERS WITH 140 DIAMETER, SATURATED PRIOR TO FILTRATION WITH 0.5 ml OF A 10% GELATIN SOLUTION

Virus type	No. of the series	Virus titre in PFU in 1 ml ($\times 10^6$), before filtration	Virus titre in PFU in 1 ml. ($\times 10^6$) after filtration
Type I	22	13.2	7.4
	23	9.0	9.0
	24	9.2	8.9
	25	11.5	9.0
	38	3.7	3.3
	41	8.8	10.0
	42	10.0	8.4
	43	19.0	16.4
Type II	31	10.0	7.1
	33	5.5	6.4
	36	13.0	14.7
	37	19.0	12.0
	40	17.7	12.5
Type III	26	11.5	9.0
	27	18.5	13.8
	28	11.0	11.5
	29	18.0	17.3
	39	16.5	18.2
	49	13.4	14.8
	50	11.3	14.3
	51	13.3	13.7

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raw water in a metal reactor with silicic enamel coating. The results obtained with media prepared by dissolution of dry ingredients in distilled water with subsequnet diltration are in no way inferior to those obtained on a standard medium. No perceptible loss of the virus is marked follwoing filtration of 50-80 litres of attenuated Sabin's virus via an asbestos"S" type filter, with 140 mm diameter, and preliminarily saturated with 0.5 ml. of a 10% gelatin solution.

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Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

BIBLIOGRAPHY.

1. Sabin, A.B. J.Am.Med.Ass.,1956,162:1581;
J.Am.Med.Ass.,1957,164:1216; Brit.Med.J.,1959,1:663.

2. Chumakov,M.P.,Gagrina,L.V.,Lashkevich,V.A.,Dzagurov,S.G.,
Ralf,N.M.,Fleer,G.P., Voroshilova,M.K.,Robinson,I.A.
Problems of Virology,1959,5,529.

3. Chumakov M.P., Voroshilova,M.K.,Vasilieva, Bakina,M.N.,
Dobrova,I.N.,Drozdov,S.G., Podsedlovsky,T.S.,Kostina,K.A.,
Shirman,G.A., Ashmarina,E.E., Yankevich,O.D.,Uspensky, Yu.S.
Problems of Virology, 1959,5,529.

4. Chumakov,M.P. and collaborators. On Mass Peroroal Immunization
of the Population in the Soviet Union with live
Poliovirus Vaccine from Sabin's strains. Report 2,
published by the AMS USSR Institute for Poliomye-
litis Research,1960,77 p.

5. Melnick J.L.Ann.N.I.Acad.Sci.,1955,61,4,p.754-773
" Bull. Wed.H.O., 1956,14,1,p.129-146.

6. Instructions for Preparation and Control of live vaccine from
Attenuated Poliovirus Strains. Manuscript, 1959.

7. Dubecco R.Proc.Nat.Acad.Sci.,1952,38,8,747-752.
J.Exp.Med. 1954,99,2,p.167-182.

8. Hsiung G.D.,Melnick J.L.J.Immunol.,1957,78,p.128.
Virology 1955,1,p.533.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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STAT

EXPERIMENTAL DATA ON THE POSSIBILITY OF INCLUDING LIVE POLIOVIRUS VACCINE INTO CANDY AND ORGANIZATIONAL PROBLEMS OF DRAGEE-CANDY WITH LIVE VACCINE MANUFACTURE

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In accord with a decision of the USSR Ministry of Health during 1960 it is necessary to carry out three to four feedings of the live vaccine to the total population of 2 months to 20 years of age, that is, about 77 million people. Specific poliomyelitis prophylaxis on such a scale during one year in a large country is possible only provided the use of the vaccine is very simple and convenient, for example, in the form of candy or some other pleasant food product. In many areas of this country there are no facilities for filling of the liquid vaccine as we used to do it before large-scale vaccination. Even such a simple procedure as preparation of 10-fold dilutions of the vaccine with water or salt solution and distribution of the vaccine in 2 drops with eye pipette caused some difficulties at vaccination clinics during mass poliomyelitis vaccination programs.

For these reasons we investigated possibilities of including Sabin live poliovirus vaccine into candy mass. First of all it was necessary to test preservation of the live vaccine virus in solutions of food sugar and in mixtures of different sugars used for candy manufacture. Experiments were made to test the effect of different temperatures on titers of vaccine poliovirus, that is preservation of vaccine virus in sugar solutions was tested at $+4^{\circ}C$ and $+22^{\circ}C$; virus kept at $-20^{\circ}C$ served as control.

Methods. In the first set of experiments the effect of 10%, 25% and 50% solutions of food sugar on type III vaccine virus (Leon $12a_1b$) at $+4^{\circ}C$ and $22^{\circ}C$ for 10 days was studied. Aliquots of type III vaccine (100,000 TCD_{50}) were added to 1 ml of the corresponding sugar solution. Half of the tubes with virus-sugar mixture was put into thermostat at $+22^{\circ}C$, the other half into refrigerator

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at +4°C. At 3,7 and 10 days these mixtures were tested in trypsinized monkey kidney cell cultures by the cytopathogenic effect. Control was included in each test consisting of similar titrations of type III vaccine virus of the same lot stored at -20°C and also virus-sugar mixtures kept for 1 hour after manufacture at room temperature. The results of one such experiment are presented in Table 1.

Table 1. - Preservation of type III vaccine virus (Leon $12a_1b$) in sugar solutions at+4°C and+22°C (titers are expressed as reciprocal log of terminal dilution /10^x/ producing CPE).

	Control		+4°C			+22°C		
	-20°C	Contact 1 hour at room t°	Period of storage (days)					
			3	7	10	3	7	10
Virus	7.3	-	7.2	7.7	7.7	7.3	7.7	7.2
Virus+50% sugar solution	-	7.2	7.3	7.7	7.7	6.97	7.3	7.4
Virus+25% sugar solution	-	7.0	7.03	7.7	7.7	7.2	7.2	7.3
Virus+10% sugar solution	-	7.3	7.5	8.0	7.2	7.3	7.3	7.3

In a number of similar experiments it has been shown that neither sugars nor food dyes used in dragée-candy manufacture have any effect on titers of Sabin vaccine strains and therefore can be used in the manufacture of candy with the live vaccine. As an illustration of experiments along these lines fig.1 shows graphical-

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ly the results of one such esperiment in which two models of candy mass of the following composition were tested:

The activity of the vaccine virus mixed with candy mass, with 50% sugar solution and with powdered glucose was tested after 20 days of storage at $4^{o}C$ (refrigerator) and $22^{o}C$ (thermostat). The vaccine virus was titrated in monkey kidney cell cultures by the cytopathogenic tube test.

As is seen in Fig.1, different kinds of sugars and their combinations did not cause any marked changes in virus titers. The titers changed only after long storage at room temperature. In this experiment the titer declined only after 10 days of storage at room temperature; titration at 14 days showed 1 $\log_{10}$ decline compared with the original titer. At 20 days the loss of vaccine virus in sugars at room temperature was over 2 logs while control virus at $4^{o}C$ still had the original titer or one very near to it.

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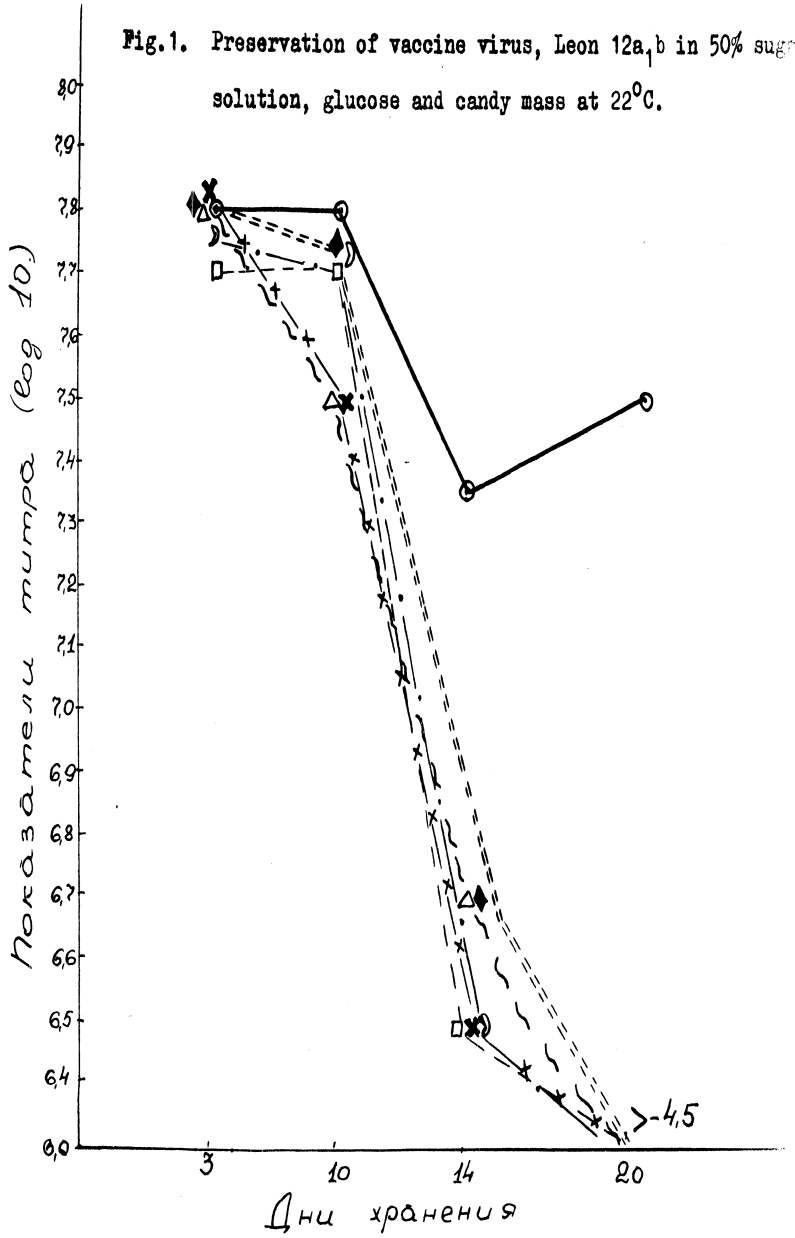
Fig.1. Preservation of vaccine virus, Leon 12a$_1$b in 50% sug[illegible] solution, glucose and candy mass at 22°C.



Legends:

0 - virus at+4°C

Δ - " "+22°C

X - Virus + 50% sugar solution at+22°C

□ - virus + glucose at+22°C

♦ - virus + candy model N 1 at+22°C

[illegible] - virus + candy model N 2 at+22°C

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Thus, our experiments have demonstrated satisfactory preservation of the vaccine virus in solutions of food sugars, in powdered glucose and in candy mass at+22°C for 7-10 days, not longer. For longer periods the vaccine virus was satisfactorily preserved at+4°C.

These first data allowed to turn to the elaboration of technology for the manufacture of special candy pomadka with live poliovirus vaccine to be tested in people (determination of establishment and immunologic activity of the live vaccine in candy form). In collaboration with All-Union Scientific Research Institute of Candy industry technological conditions for the manufacture of candy with vaccine were developed. Experimental samples of the candied vaccine were manufactured with candy model N 2 as its composition permitted more even mixing of the liquid vaccine with half-finished product. The whole manufacture process of an experimental lot of the candied vaccine was carried out at a temperature about+32°C to avoid thermal inactivation of the vaccine virus.

For first lots of the candied vaccine type I (3,280 inoculation doses), type II and III (324 inoculation doses of each) vaccine viruses and trivalent vaccine (48,500 inoculation doses) were used.

First lots of the candied vaccine were used during large-scale vaccination program in the town of Klin, Moscow region, in spring 1959. Data on quite regular establishment in children of the vaccine viruses ingested in candy and on satisfactory serologic shifts in the vaccinated are presented in a separate communication (Fleer G.P)

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The results obtained in experimental trials of the candied vaccine gave ground for wider use of this new form of the vaccine.

The experience of pomadka-candy manufacture, however, revealed certain inconvenience of pomadka, namely, much manual labour at manufacture, at packing because of difficulties in distributing the final product in small packages; besides, candy mass sometimes melted on storage, and there were some other inconveniences. Therefore the Institute of Candy industry suggested a new recipe for including the vaccine into dragee-candy which is manufactured on a large scale at a large factory.

During the process of dragee-candy manufacture the vaccine is thoroughly mixed with syrup cooled to+25°C The whole process of candy manufacture in special roller boilers is carried out at+25°C, not higher, and pH in the range of 6.8-7.2.

During an hour or an hour and a half a strictly definite quantity of syrup with the vaccine is being evenly distributed, with the addition of sugar powder, into approximately 30,000 crystal granules (sugar granules). Then the resulting spherical dragee-candies are covered in the same boiler with external sugar-fatty-wax layer preventing them from drying.

The amount of live poliovirus vaccine introduced into candy mass varies in different lots depending on virus titer from 50,000 to 350,000 TCD_{50} of the virus per one dragee-candy weighing 1 gm,

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and, as a rule, averages 100,000 TCD_{50}. The weight of individual candies may vary to ±15 per cent which is not very important for the vaccine dosage in the dragée.

Regular titration of vaccine viruses included into dragée-candy demonstrated that they are well preserved at -20°C for periods up to 3 months without any change, at+4°C up to 30 days without significant change and at+22°C for 3 to 5-7 days. Corresponding data on dragée-vaccine titration after storage at different temperatures are presented in separate communications (Dzagurov S.G., Shmeleva G.A.; Voroshilova M.K., Lashkevitch V.A. and others).

In September-November 1959 vaccination of children with live vaccine in dragée-candy was carried out (Voroshilova M.K. and others) and good results were obtained.

As the vaccine virus has been shown to be well preserved in dragée-candy, large-scale manufacture of dragée-candy with the live vaccine was immediately organized at Moscow "Marat" candy factory. Moscow City Council of National Economy helped to organize dragée-vaccine manufacture, and in short time its production reached 3 million doses per day.

In the fall of 1959 over 2,500,000 triple inoculation doses of live poliovirus vaccine in dragée form were distributed in Georgia, Azerbaijan, Armenia and Khabarovsk region of the RSFSR.

As could be expected, the dragée-vaccine proved to be most convenient for mass immunization and was completely approved of both by medical workers carrying out immunization programs and by vaccinees themselves.

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Vaccination programs have been greatly speeded up. In some towns and regions daily number of vaccinations given reached 300,000-450,000. In carrying out vaccinations with drageé-candy it has become possible to enlist cooperation of teachers in children's institutions and other non-medical workers in addition to medical personnel, which facilitates the realization of vaccination programs considerably. In winter drageé-candy with the vaccine is shipped in ordinary package, and in warm seasons in containers on ice by air and is brought for intermediate storage to cold stores of food enterprises or directly to sanitary-epidemiological stations.

At present, according to preliminary data, over 150 million inoculation doses of the live vaccine in dragge form have been manufactured and distributed all over the country. By May, 1960, second feedings and, in a number of places, third feedings with drageé-vaccine will be completed. The program to immunize 52 million people up to 20 years of age before July 1960 may be expected to be exceeded thanks to the fact that the vaccine in candy makes it possible to carry out vaccination programs in many areas of the country simultaneously.

Strict keeping of the instruction on shipment of the vaccine on ice (in spring-summer season) and storage at sub-zero temperature until use but not longer than 3 months must become a necessary requisite for the proper use of the live vaccine in drageé-candy.

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Summary.

Experimental studies revealed the possibility to include vaccine poliovirus strains into candy.

Examination of the establishment and immunogenic potency of the live vaccine in the form of pomadka-candy and drageé-candy gave grounds to large-scale introduction of the candied vaccine into practice of poliomyelitis immunization. The vaccine in drageé form does not rule out the use of the liquid vaccine, but it facilitates and speeds up vaccination procedure under certain circumstances and in certain regions of the country where the liquid vaccine can not be used.

Large-scale manufacture of the live poliovirus vaccine in drageé-form has been organized. This makes it possible to provide regular supply of the live vaccine to all demands and to carry out extensive programs of large-scale oral immunization throughout the entire country in 1960.

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EXPERIMENTAL VERIFICATION OF ADAPTABILITY AND IMMUNOGENECITY OF LIVE POLIOVIRUS VACCINE PRESENTED IN THE SHAPE OF PASTY CANDIES

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During summer 1959 mass immunization of children against poliomyelitis was carried out in the city of Klin, Moscow region. As inoculant served an experimental batch of pasty candies containing trivalent vaccine prepared from the strains attenuated by A.B.Sabin (2).

Tests previously effected under laboratory conditions proved the vaccinal virus to preserve its properties quite well inside the sweetmeat (1.2). In this experiment, therefore, we were primarily interested in the practical possibility of employing poliovirus-containing candies.

It is familiar that a number of authors, viz;- Sabasso V (3), Embil (4), Leúnda (5) have used liquid poliovirus vaccine in gelatin capsules for peroral immunization, which showed good adaptation of the vaccine in the intestine. The vaccine-containing candies are advantagious in that their very aspect is attractive to children, while the members of the local medical staff are thus able to realize the program of mass vaccinations without much trouble and delay.

In the city of Klin pasty candies with vaccine were used in immunizing a total of 21.886 children (see table 1).

Table I.

DISTRIBUTION OF THE VACCINATED ACCORDING TO AGE-GROUPS.

	2-6m	6m-1 year	1-3y	4-6y	7-9y	10-12 years	13-15 years	Total
Inoculated with live vaccine	879	1026	5075	4957	3956	3407	2586	21886
Including: immunized previously with killed vaccine	-	46	1413	2366	497	-	-	4322

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All the children, regardless of the previous inoculations against poliomyelitis, were vaccinated twice with live trivalent vaccine in the shape of pasty candies, the interval between the first and second immunizations comprising one-one and a half months. Jundging by the data furnished by the city sanitary epidemic station the vaccinations were not followed by any untoward reactions. To perform pertinent virological and serological examinations about 100 children were selected from among those who had not been previously subject to immunization with the Salk vaccine. At the time of examinations the bulk of children were aggregated in collective bodies (creches, kindergartens, pioneer camps).

From among the vaccinated 94 subjects underwent serological examinations. The blood was taken before vaccination,one month after the first, and two months following the second immunization. The titration of the double and triple sera was performed by color tests with the suspension of cells taken from a trypsinized monkey kidney.

Feces samples were taken from 119 children. They were collected twice prior to immunization and every week in the course of the first month after the primary vaccination. The virus was isolated in the test-tube culture of a trypsinized monkey kidney.

In typing of the fecal strains a procedure of simultaneous titration and typing was adopted, which ran according to the following scheme: there is prepared suspension of fecal matter in a series of dilutions with the raio of 0.5 comron logarithm. 0.5 ml of each dilution is combined with a mixture of two immune sera of the types I + II, or I + III and II + III, containing 20 serum units of each type in the final dilution. The mixtures were left standing for one hour at room temperature

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to achieve contact. For inoculation 0.2 ml of the mixture was taken, comprised of virus + serum. The presence of one,two,or three virus types in the fecal samples was determined by the cytopathogenic effect in the cellular cultures in diverse combinations of the sera of various types; parallel with this is set the titre of the virus.

INVESTIGATION RESULTS.

1. Adaptation of the vaccinal virus introduced into the intestinal tract of children together with pasty candies.

Of the total of 119 examined 29 excreted the virus before vaccination. The data below refer to children with no cytopathogenic agents in pre=vaccinal samples.

Table 2.

THE FREQUENCY OF THE VACCINAL VIRUS EXCRETION IN CHILDREN IMMUNIZED WITH THE TRIVALENT ATTENUATED VACCINE IN THE SHAPE OF PASTY CANDIES

The city of Klin,1959.

Age=groups:	Examined: children	Aver. numb.of fecal samples	Total of fecal samples in the given group	Virus excretion: Number of children	% of excretions	Positive samples	% of excretions
4 m.-3 year	30	4	118	28	93.0	78	66.0
3 - 7 years	12	3	38	10	85.0	25	66.0
7-15 years	48	3	158	43	89.0	97	61.0
T O T A L	90		314	81	90.0	200	63.7

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As seen from table 2 the tests of candies with vaccine for the frequency of the vaccinal virus adaptation in the immunized rendered quite satisfactory results. The virus excretion was established in 81 of the 90 children under examination (91%). The indices of the virus-carrier state within individual age-groups were: in the age bracket of 3 months-3 years - out of 30 examined children - 28 excreted the virus; in the group of 3 years-7 years the excretion percentage amounted to 85, while in the bracket of 7-15 years the virus was revealed after vaccination in 43 subjects out of the total of 48 (89%).

The typing of the fecal viruses proves that of the second type to be excreted most frequently. Following investigation of 44 fecal samples the virus of the first type could be isolated in 22 instances (50%), of the second type - 39 (90%) and that of the third type-in 23 samples (52%).

Graph No.1 includes indices of the titres for the viruses isolated from the feces (at the rate per 1 grm of the excreta) in children Sh.,N.,K.,M.,G.,P.,M.

The mean arithmetical titre for viruses following examination of 20 fecal samples amounts for the first type -$10^{2.3}$, for the second - $10^{3.5}$ and for the third type- $10^{2.8}$.

There could be noted a definite correlation between the indices showing the virus multiplication in the intestinal tract of the vaccinated- on the one hand, and the development of antibodies in the blood of the same children - on the other.

2. Serological Shifts in the Blood of the Vaccinated.

The results of serological investigations are listed in tables 3,4 and 5. Of interest is the group of triply negative children (table 3). Of 19 subjects, who prior to vaccination had no antibodies to the three types, after single immunization

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with t.'valent vaccine in the shape of candies- two remained triply negative, 13 subjects acquired antibodies to the first type, 16- to the second and 8 - to the third type.

The increase in the number of subjects with antibodies following vaccination was satisfactory with reference to antibodies of the I type=+59.5% and second type= +50.0%, and not quite so to the III type = +36.5%. If the shifts be calculated according to groups only, globally, without taking account of antibodies before vaccination, one can see that in 81.2% there appeared antibodies to the I type, in 84.5% - to the II , while in 51.6% of cases the development of antibodies to the III type could be established.

T a B l e 4.

MEAN GEOMETRIC TITRES OF ANTIBODIES IN CHILDREN IMMUNIZED WITH TRIVALENT LIVE VACCINE IN CANDIES, TWO MONTHS AFTER INOCULATION

(Klin, Moscow region, color test)

Groups (before vaccination)	Total number	I type		II type		III type	
		Before Immunizat.	After Immunization	Before	After Immunization	Before	After Immunization
1. "Triply seronegative	19	0	21	0	39	0	3
2. "With incomplete set of antibodies" ..	25	7	158	9	223	5	39
3. "Triply positive"	50	60	158	52	239	32	128

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The data listed in table 4 indicate that mean geometrical titres of antibodies to the second type in the group of the triply negative are three tires in excess of the indices for the first type and 13 times as high as the mean geometric titre to the third type.

In the groups with incomplete set of antibodies and in the triply positive subjects the indices for the mean geometric titre to the second type are also far above those for the two other poliovirus types.

In order to assess the results consequent upon immunization with trivalent vaccine in the shape of candies we have confronted them with the data supplied by I.N.Dobrova (see Report No.2,p. 29) relative to serological examination of children in the Estonian SSR, following their immunization with trivalent live vaccine prepared from the A.B.Sabin's strains.

In general,the comparison has shown a great deal of similarity in the immunological response displayed by both groups, expept for that to the vaccine of the III type, a mention of this having been already made before (table 5).

Thus, summarizing all that has been said here before, one can point out that, following the use of candies containing trivalent poliovirus vaccine there can be observed regular adaptation of the vaccinal strains in the intestinal tract of children and serological changes, very close to those noted in subjects immunized with liquid trivalent vaccine.

The use of candies with live vaccine in mass immunization demonstrated their definite advantages over the employment of liquid vaccine.

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C O N C L U S I O N S

1. Data are presented illustrating virological and serological examinations of the immunized with an experimental lot of trivalent vaccine in the shape of pasty candies.

2. Evidence is brought of regular adaptation of vaccinal strains introduced into the intestinal tract of children together with candies.

3. The comparison of immunogenecity produced by the trivalent vaccine contained in candies with that dispensed in liquid form has demonstrated a great similarity in their general immunological response to the vaccination of children with these preparations.

These data are sufficient to conclude that mass employment of poliovirus vaccine in the shape of candies is not only possible, but advisable, too.

BIBLIOGRAPHY.

1. Bezzubov, A.D., Fleer, G.P., Dzagurov, S.G, Chumakov, M.P.: Experimental data on the possibilty of enclosing live poliovirus vaccine in candies / Maniscript=papers presented at the IV Conference of the Institute for poliomyelitis research.

2. Chumakov, M.P. and coll.: Mass oral immunization of the population in the USSR with poliovirus live vaccine. Report No.2 Publication of the Institute for poliomyelitis research, Moscow, 1960, p. 77.

3. Cabasso, V., 1959 : Cumulative testing experience with consecutive lots of oral poliomyelitis vaccine. Conference on live poliovirus vaccine. Washington

4. J. Embil, 1959, A Clinical and serological study of the response of Cuban children to oral vaccination with attenuated poliovirus vaccines. Conference on live poliovirus vaccines Washington

5. J. Leúnda, 1959: Programa de vacunation en masa contra la poliomielitis efectuada en Montevideo con virus vivos atenuados Conference on live poliovirus vaccines. Washington.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

6. Dobrova,I.N. (cited according to Chumakov with coll. - Report No. 2, Publication of the AMS Institute for poliomyelitis research, 1960,Moscow, pp.29).

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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T A B L E 3.

The antibody development in children aged from 4 months to 15 years with incomplete set of antibodies before the vaccination and two months after administration of live trivalent vaccine in the shape of pasty candies.

Antibodies before vaccination (1 sample)	Antibodies 2 months after immunization								2d sample with antibo		
	000	00+	0+0	0++	+00	+0+	++0	+++	1+	II+	III+
000 19 h. 43,1%	2 10,5	1 5,3	2 10,5	1 5,3	-	-	7 36,8	6 31,6	13 68,4	16 84,2	8 42,1
00+ 3 h. 6,8%	-	-	-	-	-	1 33,3	-	2 66,6	3 100,0	2 66,6	3 100,0
0+0 4 h. 9,0%	-	-	-	-	-	-	1 25,0	3 75,0	4 100,0	4 100,0	3 75,0
0 ++ 6 h. 13,6	-	-	-	-	-	-	-	6 100,0	6 100,0	6 100,0	6 100,0
+00 3 h. 6,8%	-	-	-	-	-	-	2 66,6	1 33,3	3 100,0	3 100,0	1 33,3
+0 + 4 h. 9,0%	-	-	-	-	-	-	-	4 100,0	4 100,0	4 100,0	4 100,0
++0 5 h. 11,3%	-	-	-	-	-	-	1 20,0	4 80,0	5 100,0	5 100,0	4 80,0
Total with the deficit of antib. 44 h. 100,0%	2 4,5	1 2,2	2 4,5	1 2,2	-	1 2,2	11 25,0	26 59,0	38 86,4	40 90,9	29 66,0

II. The number of children with antibodies (out of 44).

: Before vaccination	: After vaccination		: Increase in %
I+ 12 h.-27.2%	38 h.	86.4%	59.2%
II+ 18 h.-40.9%	40h.	90.9%	50.0%
III+ 13 h.-29.5%	29 h.	66.0%	36.5%

III. The number of children without antibodies (out of 44).

Before vaccination	After vaccination	
	Acquired antibodies:	Including those who aquired :antibodies in the group of : "triply negative".
I_0	32 h.	26 h. -81.2% 68.4%
II_0	29 h.	25 h. -84.5% 84.2%
III	31 h.	16 h.-51.6% 51.6%

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TABLE 5.

COMPARATIVE DATA OF A SEROLOGICAL EXAMINATION COVERING SUBJECTS IMMUNIZED WITH LIQUID TRIVALENT VACCINE AND TRIVALENT VACCINE CONTAINED IN PASTY CANDIES.

Combinations of the antibody types

Trivalent liquid vaccine (x)				Trivalent vaccine in pasty candies (xx)			
Before vaccination	Sum=total with antibodies after immunization			Before vaccination	Sum=total with antibodies after immunization		
	I+	II+	III+		I+	II+	III+
000 I3 h. 26,5%	8 6I,5%	I0 76,9%	I0 76,9%	000 I9h. 43,I%	I3 68,4%	I6 84,2%	8 42,I%
00 + 4 h. 8,2%	3 75,0%	3 75,0%	4 I00,0%	00+ 3 h. 6,8%	3 I00,0%	2 66,6%	3 I00,0%
0+0 I0 h 20,4%	8 80,0%	I0 I00,0%	7 70,0%	0+0 4 h. 9,0%	4 I00,0%	4 I00,0%	3 75,0%
0 ++ I2 h. 24,5%	9 75,0%	I2 I00,0%	I2 I00,0%	0 ++ 6 h. I3,6%	6 I00,0%	6 I00,0%	6 I00.0%
+00 4 h. 8,2%	4 I00,0%	4 I00,0%	3 75,0%	+00 3h. 6,8%	3 I00,0%	3 I00,0%	I 33,3%
+0+ 3 h 6,I%	3 I00,0%	3 I00,0%	3 I00,0%	+0+ 4h. 9,0%	4 I00,0%	4 I00,0%	4 I00,0%
++0 3 h. 6,I%	3 I00,0%	3 I00,0%	2 I00,0%	++0 5h. II,3%	5 I00,0%	5 I00,0%	5 I00,0%
49	38	45	4I	44	38	40	29
I00,0%	77,5%	9I,8%	83,7%	I00%	86.4%	90.9%	66.0%

Rise in the number of antibodies		Rise in the number of antibodies	
I +	+ 57.I%	I +	+ 59.2%
II +	+ 40.8%	II +	+ 50.0%
III +	+ 44.9%	III +	+36.5%

(x) According to Dobrova, 1959, Estonia. (xx) According to Fleer, 1959 Klin.

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Detection of Intranuclear Inclusions and Histochemical Changes in Spinal Cord Cells of Monkeys with Unapparent Infection, Caused by A. B. Sabin's Attenuated Strains

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A. M. S. U S S R

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In the recent period an interest in the problems concerning forme fruste and subclinical forms of viral infections has risen considerably.

The studies devoted to the latent forms of infections appearing in natural conditions, as well as in experiments, have not only a theoretical, but a practical significance as well. They help to understand the role of these infections in the pathology and epidemiology of corresponding diseases. Experimental morphological investigations of the latent infections, exposing the most peculiar cytological changes due to the specificity of the intracellular growth and multiplication of viral particles, make it possible to solve several problemsin ms in respect to the pathogenesis of the disease.

A latent course of poliomyelitis has a special interest for physicians, who are using attenuated strains of poliovirus in ordinary practice.

Our paper presents a morphological study on a latent infection in monkeys, caused by the introduction of attenuated strains of poliovirus into their body. These strains were proposed by Albert Sabin for preparing a live poliovaccine. Attenuated poliovirus strains possess a decreased neurotropic and invasional effects and after introducing them into the body of monkeys (Macacus Rhesus) give neither clinical, nor morphological manifestations of poliomyelitis except in a few cases.

The biological essence in the attenuation of these strains and, namely, their interrelationship with the nerve cell have not been studied as yet. Not excluding the possibility of an unapparent and mild course of the latent infection, we had set a task to reveal peculiar changes in the

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in the nerve cells, which appear after inoculating the virus directly into the nervous tissue.

From this aspect we studied the central nervous system in 30 monkeys, infected intracerebrally or intrspinally with attenuated strains of poliovirus. For histological investigations we used ordinary stains (hematoxylin and eosin and Nissl's staining method), some of the histochemical reactions (ribonucleinic acid - RNA- after Brachet and desoxiribonucleinic acid - DNA - after Feulgen) and several special cytological techniques for the detection of intranuclear inclusions (Unna's staining method and staining after Romanovsky and Hiemsa; for this purpose our material was fixed in Bouin's fixative). Our control group included the brain and spinal cord of I5 intact monkeys, which were studied by the same histological and histochemical methods. It should be mentioned, however, that our study was performed on monkeys sacrificed on the 2Ist day following experimental infection, and therefore, we did not have an opportunity to reveal all the morphological changes developing in dynamics. Of the 30 experimental animals 20 were infected intracerebrally. All of them displayed no characterestic morphological manifestations of poliomyelitis. Of the I0 remaining monkeys infected intraspinally 6 had a morphological evidence of poliomyelitis.

Upon fine microscopic investigation of the central nervous system in 24 of the 30 monkeys, infected with the attenuated virus, in the neurons of the maximally impaired regions, along with mild structural changes in cytoplasm and nucleus, we found striking derangements in the nucleic metabolism, as well as sufficiently well pronounced intranuclear eosinophilic inclusions, described in detail by numerous

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investigators, and found to be specific for the nerve cells impaired by poliovirus. These inclusions were found in I7 of the 20 animals infected intracerebrally and in ~~0f~~ 7 of the I0 infected intraspinally. Three of these seven had shown a characteristic and a complete morphological picture of poliomyelitis.

The intranuclear eosinophilic inclusions with a regular round form, from one to three in number, were found with great constancy in the nuclei of spinal cord motoneurons, and more rarely in the nuclei of the medulla oblongata and mesencephalon neurons. The size of these inclusions varied from 0.5 to 3.0 microns in diameter (Fig I and 2).

Phasocontrast microscopy distinctly revealed intranuclear inclusions which could be readily differentiated from the other nuclear patterns. Usually they were recognized by a greenish fluorescending radiation and by the presence of a light rim on its perifery (Fig 3).

The presence of intranuclear inclusions, characteristic for poliomyelitis in monkeys and human beings, as it is considered by many authors,(Covell W.P., Hurst E.W., Sabin A., Bodian D., Popova L.M. and Avokyan A.A. and oth.), indicates that the attenuated virus had penetrated into the nerve cell, started to multiply, and that the infection is latent in its course. This is substantiated by constant observations of structural changes of the cytoplasm and nucleus, as well as by the presence of marked disturbances in the nucleic metabolism of neurons, where eosinophilic inclusions are usually revealed. The changes in the nucleic metabolism of nerve cells due to the interaction of the cell and the poliovirus, are described in detail in the pertinent literature (Hyden H.,

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Einarson N., Casperson, T., Kedrovsky, B.V., Avokyan,A.A. and Popova,L.M.).

As a result of viral parasitism in the nerve cell, the metabolism of the neurons changes to such a degree,that it affects their state of physiological balance, and ~~in~~ leads to the death of the cell, when the process becomes irreversible

In sections stained after Brachet for ribonucleic acid we were able to reveal striking deficiency in the cytoplasmic ribonucleic acid of neurons, which were found in a state of a total or central tigrolisis. Apparently, the cause of derangement in the structure of Nissl's substance lies in the impairment of RNA metabolism.

In some cells we observed slight and diffuse eosinophily of the nucleus, while in several cells the large lumps of Nissl's substance rich in RNA were noted. The changes in the amounts of desoxiribonucleic acid - DNA- were not demonstrable. No doubt, that just described changes in nucleic metabolism in neurons are due to the parasitism of attenuated poliovirus, introduced into the nervous system. They indicate on the survival of virus for ~~not~~ a period not less than 21 day, or may be significantly more, after the penetration into the central nervous system of monkeys. All this seems to be in agreement with the recent observations of Bodian, who was able to isolate poliovirus from the nervous tissues.

Attenuated strains of virus, introduced intracerebrally, being incapable of producing any degenerative or inflammatory changes in the central neryous system, cause, however, well pronounced derangements in the metabolism of the host's nerve cells during the process of selfreproduction. It is still not clear,whether the accumulation and multiplication of virus

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take place only in the cytoplasm of the nerve cell, or these processes could be detected in the nucleus as well. the data recieved during the fractioning of the cellular organoids by the method of differential centrifugation seem to confirm the vieww of Hyden and Bodian, who found that the significant concentrations of virus are present not only in the cytoplasm bu also in the nuclear fractions of the nerve cells.

The same question arises in respect to the intranuclear inclusions: is it a place of viral multiplication or it is only a form of response to the penetrated virus? It is doubtless, however, that these intranuclear inclusions have a specific morphological evidence of polioinfection and could be demonstrated not only during the full clinical and morphological manifestation of poliomyelitis, but in the latent forms of infection, caused by the attenuated poliovirus as well. Whereby, in the course of the latent infection they are found significantly easier and more frequently. This can be explained, if we will consider that in the case of a pronounced poliomyelitis the nerve cells become impaired very fastly with the development of necroses and degenerations. All this makes it difficult to reveal intranuclear inclusions, which as it is well known, are demonstrible in the cells with rather minimal changes.

Quite possible , that intranuclear inclusions have some relations to the defense mechanisms of the cell , which increases its resistibility and gives a cell an ability of creating new symbiotic relations with the virus.

For...."The essence of every latent period, independently of the used term for it(incubation, latency, remission), consists in the compensatory and adaptive mechanisms and responses, which recieve more and more significance, if the

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main pathological process develops more slowly."

(Davydovsky).

Conclusion. I. Attenuated strains of poliovirus, proposed by Albert Sabin for the prodution of live poliovaccine, having markedly decreased neurotropic and invasional properties, after introducing them into monkeys, do not give any clinical or morphological signs of poliomyelitis, witha few exceptions. 2. On fine microscopic investigation of the central nervous system of the infected monkeys in the neurons of the maximally impaired by the virus regions, together with slight structural changes in the cytoplasm and nucleus it was possible to reveal a significant derangement in the nucleic metabolism and the presence of well demonstrable intranuclear inclusions, which have an eosinophilic appearance. The characteristic impairment of the nucleic metabolism as well as the evidence of intranuclear inclusions, which represent one of the most specific morphological signs of the affection of nerve cell by the poliovirus, confirms a view that the virus has penetrated into the nerve cell, started to multiply there , and that the infection has a latent course. The indicated changes show that they are the sequeles of the direct interaction of the nerve cell with the virus, and that these changesare related to the specificity of the intracellular growth and multiplication of the viral particles.

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Interference between different strains of polioviruses in the light of general theory of microbial antagonism.

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Viruses constitute a group of microbes, hence regularities common to microorganisms should be applicable to them. Besides, viruses like other groups of microbes have some specific properties due to peculiarities in their biology.

Both general laws concerning microbes as a whole, and individual regularities, peculiar to bacteria and some other groups of microbes have been studied much better than regularities of virus biology. The explanation lies in the fact that virology is a younger branch of science than bacteriology and microbiology. Hence, approach to the study of this or that problem of virology should be based, in our opinion, on what is already known in regard to other groups of microbes, first of all bacteria. It was this approach that contributed to the progress of virology.

Many years have been devoted by one of us (Peretz) to studies of microbial antagonism and to virology in recent years; and in these studies we could not help paying attention to interference phenomenon between viruses. After examination of data reported in literature on this phenomenon we came to the conclusion that mechanisms of interference between viruses and of bacterial antagonism are principally similar, and that differences in their manifestations are due to specific character of their reproduction, viruses multiplying in host cells, bacteria in artificial nutrient media.

There are many diverse opinions concerning the nature

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and mechanism of interference. Some investigators believe that interference between viruses comes to their competition in which one of the viruses breaks normal course of metabolic process thereby depriving the other virus of necessary metabolites. Such views are most close to the explanation of interference mechanism by antagonistic relationships between viruses. Other authors think that inactivated virus may also be able to interfere with live microbes. Some authors are of the opinion that multiplication of the blocked virus is prevented by inflammatory reaction caused by the blocking virus, others think that the blocking virus activates antiviral substances in the cell which prevent multiplication of the blocked virus. Some investigators, discussing interference phenomenon point to its association with immune status of the body; others, on the contrary , believe that interference is not an immunological phenomenon.

We considered it necessary for the elucidation of correctness of our assumption on similarity between mechanisms of virus interference and bacterial antagonism to carry out tests in vitro in tissue culture to rule out any influence of the host.

The technique of our tests was as follows: two different poliovirus strains were mixed in definite proportions by quantity and inoculated into tissue culture tubes (monkey kidney cell or Hep-2 cells), which were incubated at 37°C. After development of the cytopathogenic effect, the quantity of each of the interacting viruses was determined by titration of virus-containing culture fluid in which one of the viruses was neutralized by type-

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spesific serum. These tests were done by generally accepted virologic methods, with controls included in each test.

Many microbiologists deny the existence of intraspecies microbial antagonism. It is probably for this reason that virologists speaking of competition between viruses (e.g. elimination of wild poliovirus strains by vaccine strains from the intestinal tract) do not call this phenomenon antagonism.

Our studies have proved the existence of intraspecies antagonism: testing the effect of strain Bact.coli M-I7, possessing high antagonistic index, on other strains of E.coli with less marked antagonistic properties we observed not only inhibition of the latter by M-I7 strain but their complete elimination.

In order to find out the existence of virus intraspecies antagonism we studied antagonistic relationships between some poliovirus strains. As an illustration we shall describe an experiment with type II Ovchinnikov strain and type III Sabin vaccine strain. A mixture of these two strains was inoculated into Hep-2 cell cultures, I00 TCD_{50} of each. After complete development of the cytopathogenic effect it was found that Ovchinnikov strain multiplied to I,000,000 TCD_{50}. If such effect of the former strain on the latter continues in further passages it will lead to complete elimination of Sabin strain.

The data obtained in this and other similar experiments allow to conclude that there exist antagonistic relationships between viruses and that these relationships may be observed between strains belonging to the same species.

In our attempts to approach the elucidation of mechanism

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of virus antagonism we tried to correlate regularities of virus antagonism and those of other microbes.

The mecganism of microbial antagonism is complicated and diverse. Mechanism of Escherichia coli antagonism was studied most thoroughly. According to some authors antagonistic effect of E.coli on different microbes is associated mainly with the following factors: capacity of microbe-antagonist to alter pH of the medium and to set an oxidation-reduction potential most favourable for its development; taking away from the medium in which microbes are multiplying together of nutritional substances necessary for one of the microbes, and depriving them of oxygen. Some investigators attach especially great importance to multiplication rate of microbe-antagonist: that of interacting microbes is considered to be antagonistic which in a given medium reaches M-concentration in the shortest time[x/]. Important are also antibiotic substances excreted by microbes. But the importance of this factor is, perhaps, not as common to all groups of microbes as that of multiplication-rate.

Accordingly we made experiments aimed at finding out whe-

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x/ M-concentration (maximum microbe concentration) is a maximum number of live bacteria which can be present in a definite volume of nutrient medium. For example, in meat peptone broth M-concentration of Shigella is 300 million; different strains of E.coli have M-concentration of I to I.5 billion per I ml.

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ther some regularities established in bacterial antagonism may be applied to viruses.

The applicability of the mentioned main regularity to viruses is illustrated by the above experiment of interaction of Ovchinnikov type II strain with Sabin type III strain. In control cultures of this experiment M-concentration of Ovchinnikov strain which exerted antagonistic effect on Sabin strain, was 3I,620,000 TCD_{50} whereas that of Sabin strain was I0 times lower, 3,I62,000 TCD_{50}.

In case of interaction of bacteria with similar M-concentrations none of the species exerts any antagonistic effect on the other. In order to find out whether this regularity is applicable to viruses we made experiments with Sabin vaccine strains of the three types, M-concentration of them being more or less similar. Interaction of these strains was studied in different combinations: types I+II, I+III, II+III and I+II+III, with all these strains being taken in equal amounts (I000 TCD_{50}). It was demonstrated that in none of these combinations was any inhibition of one strain by the other observed; there was only some delay in multiplication of types I and III strains in the presence of type II strain.

Next question which we attempted to answer concerned the influence of the amount of the virus taken on the results of antagonistic interaction. For this purpose in an experiment with Sabin vaccine strains we used I000 TCD_{50} of type I and I0 TCD_{50} of type II virus. Simultaneously another experiment was set in which the

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proportions were the reverse: I0 TCD_{50} of type I and I000 TCD_{50} of type II virus. The following results were obtained: in the first experiment type I strain achived 3I6,200 TCD_{50} while type II strain only 5,495 TCD_{50}. In the second experiment type I strain multiplied only to 3I62 TCD_{50} while type II strain to 3I6,200 TCD_{50}. This indicates that the larger the amount of the blocking virus in the beginning of its interaction with the blocked one, the greater its antagonistic effect is exhibited.

It followed from these experiments that with different times of introduction, antagonistic effect will be exerted by that virus strain which was introduced earlier, as at the time of contact of the two virus strains the first will be present in this medium in greater quantity.

This was confirmed in experiments done in the following manner: tube tissue cultures were inoculated with I0 TCD_{50} of Sabin type I strain. 24 hours later I0 TCD_{50} of type II strain were added to each tube. Their interaction resulted in type I reaching I73,800 TCD_{50} and type II, introduced later, reaching only I738 TCD_{50}. In an experiment in which these strains were inoculated into tissue cultures in the reverse order, type I strain, inoculated later, multiplied only to I738 TCD_{50}, while type II strain introduced first, reached 3I6,200 TCD_{50}.

Summarizing the results obtained we can formulate the apparent regularities of antagonistic relationships between virus strains in the following way: antagonist is that of the interacting strains which in a given medium can reach the highest M-con-

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centration most rapidly. This depends both on the capacity of this strain to multiply more extensively than other interacting strains, and on its introduction into the culture in greater quantity or at an earlier time.

Preliminary conclusions of experimental investigations obtained so far are confined to the abovesaid. They confirm our initial thesis that the problem of interference between viruses should be studied in the light of general theory of microbial antagonism. The studies carried out present just the initial stage of investigations along these lines and they are important only from the point of view of statement of the question substantiated by some experiments. For the investigation of the question extensive studies are required: applicability of the evident regularities to different strains of poliovirus, to interaction of the latter with the enteric viruses (ECHO, Coxsackie), to adenoviruses, and, finally, to various other viruses, causative agents of different virus infections.

Such studies will not be only of theoretical interest, but will have some practical importance as well. Thus, for instance, the results demonstrating the capacity of poliovirus strains with high M-concentration to inhibit strains with lower reproduction capacity indicate the advisability of searching for and selecting new vaccine strains with high reproduction capacity.

One more regularity of microbial antagonism should be pointed out, applicability of which to virus antagonism should be studied. This regularity which we established in regard to microbes of normal microflora may be formulated as nonspecific character

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of microbial antagonism. It has been found out that a microbe being under given conditions an antagonist to one microbial species, usually acts antagonistically to various other species. For example, E.coli which in the intestinal tract are antagonists to dysentery bacteria, exert their effect on many other pathogenic and putrefaction bacteria present in the intestinal tract, though to a different extent. And Escherichia coli strain possessing higher antagonistic index towards one of bacterial species will exert most extensive influence on other species as well.

This regularity may be applicable to interviral antagonism. Sabin vaccine strains are known to eliminate from the intestinal tract not only wild poliovirus strains but, in a number of cases, some other enteric viruses.

According to the data regarding microbes of normal microflora, Sabin vaccine strains may be expected to exert antagonistic influence on some other viruses in the intestinal tract, particularly, infectious hepatitis virus. We consider it worth mentioning because at present there is an opportunity to check this assumption by epidemiological methods: if such is the case, immunization of millions of people in this country with Sabin live vaccine must reduce infectious hepatitis incidence to a certain extent.

All our conclusions on regularities of interviral antagonism are based on experiments done in growing tissue culture. We intentionally tried to use simplified conditions to rule out any influence of the host on virus interaction in the cell. Undoubtedly, relationships of microbes, including viruses, in the body are more complicated, affected by the host and, in its turn, exert

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some influence on the host. Therefore, in addition to more thorough investigation of the mechanism of viral antagonism in vitro, its regularities in the human body should necessarily be studied.

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Spread of vaccine virus in boarding children's institutions and households during immunization with live poliovirus vaccine

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One of the requisites of live poliovirus vaccine effectiveness is the establishment and successful multiplication of vaccine virus in the body of vaccinated persons.

We studied the dynamics of vaccine virus multiplication in the intestinal tract of vaccinated and their contacts during mass immunization of population with live attenuated poliovirus vaccine carried out in February-April, 1959, on the schedule type I - type III - type II at monthly intervals.

The surveys involved vaccinated children in children's home, nursery, kindergarten as well as unvaccinated children of these institutions who were in contact with the vaccinated. 230 children were tested, of them 102 vaccinated with live vaccine and 118 in contact with the vaccinated.

Stool specimens were collected before vaccination and at 3, 7, 14, 28, 45 days after each feeding. Thus each child was tested up to 15 times. 894 stool specimens from the vaccinated and 82k specimens from their contacts were studied virologically.

20% stool suspension was prepared and treated by centrifugation and with antibodies. Then it was diluted 10-fold up to 10^{-6}. Virus isolations were made in monolayer fibroblasts of human embryonic tissue by the usual method. Virus isolates were typed with sera obtained from Moscow Institute of Poliomyelitis Preparations.

We studied frequency and duration of vaccine virus excretion and dynamics of vaccine virus multiplication in the intestinal tract of the vaccinated and their contacts. Data on frequency and duration of vaccine virus excretion in the vaccinated are presented in Table 1.

Frequency of virus excretion in the vaccinated was found to

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be maximum (75 per cent) at 7-14 days. The duration of fecal d excretion of the vaccine virus did not exceed 45 days.

Intensity of virus excretion was estimated by determination of virus titer per 1 gm of stools. The highest titers were obtained for type I and type II viruses. Type III virus titer was, as a rule, not higher than 10^{-3}, and only occasionally titers of 10^{-4}, 10^{-5} were found. Dynamics of vaccine virus multiplication is shown in Table 2.

It is noteworthy that in the first survey done 2 days before vaccination 7 children were found to excrete different enteric viruses, of which type III poliovirus was isolated from one child, Coxsackie A virus from two children, ECHO-8 virus from one child; three of the children excreted viruses which could not by typed with available typespecific immune sera. These data are given in Table 3. The data obtained indicate in a number of cases the occurrence of interference between enteroviruses and the vaccine virus. In all these cases after immunization type I vaccine virus was excreted with some delay or not excreted at all.

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Table 1

Excretion of vaccine virus after immunization

	Type I				Type III				Type II				
Days after vaccine feeding	3	7	14	28	3	7	14	28	3	7	14	28	45
Number of children tested	102	102	100	98	101	102	100	97	98	101	95	94	90
Number of children excreting virus	38	60	75	21	46	67	64	33	24	63	57	12	5

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Table 2

Virus titer in stools at different intervals after vaccine ingestion

Stool specimen dilution	Number of children excreting vaccine virus												
	Type I				Type III				Type II				
	Days after immunization												
	3	7	14	28	3	7	14	28	3	7	14	28	45
10^{-1}	2	-	5	2	3	3	8	6	5	3	8	3	2
10^{-2}	5	1	12	11	5	8	17	12	14	15	11	4	2
10^{-3}	6	20	31	6	16	13	25	11	2	17	23	3	1
10^{-4}	20	32	25	2	15	29	12	4	3	22	12	2	-
10^{-5}	5	7	2	-	7	14	2	2	-	6	3	-	-
10^{-6}		-	-	-	-	-	-	-	-	-	-	-	-

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Table 3

Establishment of vaccine virus in children from whose stools enteric viruses were isolated before immunization

Virus isolated before immunization	Types of virus isolated at different intervals after immunization (days)											
	3	7	14	28	3	7	14	28	3	7	14	28
Poliovirus type III	-	-	I	I	I	-	-	-	II	II	-	-
Coxsackie A	-	-	I	-	III	III	-	-	-	II	II	-
Coxsackie A	-	-	-	-	-	III	III	-	II	II	-	-
ECHO-8	-	I	-	-	III	III	-	-	-	II	-	-
Untypable virus	Untypl vir.		I	-	-	-	III	-	II	-	II	-
- " -	-	-	I	-	III	III	-	-	II	II	-	-
- " -	-	-	-	I	-	III	-	-	-	II	II	-

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Comparison of data on the presence of prevaccination antibody and on frequency of vaccine virus excretion showed that, as a rule, vaccine virus was excreted in children without homologous antibody or with antibody titer not exceeding 4. Exceptions were two cases of type II and one case of type III virus excretion in children with antibody titers of 16. In the presence of antibody in high titers there was no excretion of vaccine viruses.

In parallel with vaccinated children their contacts were surveyed at the same intervals. In a number of boarding institutions different proportions of children were fed with the vaccine, for example, in children's home 65 per cent of children, in nursery No. 24 25 per cent. This proportion of the vaccinated was taken into account in the analysis of vaccine virus excretion in contacts. Data on vaccine virus excretion in contacts, presented in Table 4, show that with massive introduction of vaccine virus into a community it was excreted almost in 50 per cent of the contacts, whereas with vaccination of only 25 per cent of the population of a boarding institution only 26 per cent of the contacts excreted vaccine virus.

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Table 4

Excretion of vaccine virus in children who were in contact with vaccinated

Institutions surveyed	Type I				Type III				Type II				
	Days after immunization												
	3	7	14	28	3	7	14	28	3	7	14	28	45
City children's home (immunized 65% of 60 pers.)	-	1	17	11	5	3	6	8	8	5	9	7	4
Nursery (immunized 25% of 20 pers.)	-	1	9	15	16	7	11	20	5	4	7	7	3

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In contrast to the vaccinated vaccine virus excretion in the contacts was observed 14 days after vaccination and reached the peak at 28 days.

In addition to investigation of vaccine virus excretion in contacts living in boarding institutions we also studied the spread of vaccine virus in households under normal circumstances. For this purpose we selected a group of children living in communal flats. The children were vaccinated in children's institutions with type I monovaccine. Mothers of the vaccinated children and all children of pre-school and school ages living in the same flat but not receiving the vaccine were tested, a total of 18 contacts (12 mothers, 3 pre-school children and 3 school-children).

Here the following data were obtained. 21 days after immunization of children the vaccine virus was isolated from 5 mothers of the eleven tested. At 30 days the virus was isolated from 2 mothers and one child. At 60 days none of the contacts had any poliovirus.

The data obtained in these studies show that maximum excretion of vaccine virus in the vaccinated was observed at 7-14 days and reached 75 per cent. The correlation was noted between virus excretion and presence of homologous antibody in the vaccinated. Spontaneous enteric virus carriage had some influence on vaccine virus excretion. Excretion of vaccine virus in contacts was found to occur at later intervals than in the vaccinated and was related to the number of the vaccinated in the community. Relatively wide spread of vaccine virus among the contacts both in children's institutions and in households was observed.

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Some data on dissemination of enteric cytopathogenic viruses among healthy children in Moscow

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The problem of intestinal virus carriage of "cytopathogenic agents" in healthy children is very important now because of possible interference in large-scale oral immunization of population with live poliovirus vaccine.

Due to extensive introduction of monkey kidney cell tissue culture methods into virologic investigations during the past decade a number of investigators have been able to discover in the human intestinal tract a large and antigenically heterogeneous group of cytopathogenic agents, in addition to poliomyelitis and Coxsackie viruses.

The first six antigenic types of viruses called "orphan viruses" were described by Melnick and co-workers (Melnick et al., 1953, Melnick, 1954, 1955). These viruses were isolated both from patients with nonparalytic poliomyelitis and healthy persons.

Ramos-Alvarez and Sabin (1954, 1956) searching for avirulent poliovirus strains among healthy children isolated 365 cytopathogenic agents of which 286 were identified as poliomyelitis and Coxsackie viruses. The remaining 88 unidentified viruses named "enteric viruses" were classified into five antigenic groups which differed considerably from the six antigenic groups previously established by Melnick.

Hammon and co-workers (1955, 1957 a, b) in surveys of normal people in the Philippine islands isolated 204 agents of which 41 were identified as polioviruses and of the remaining 163 agents two antigenic groups were formed. Thus already by 1955 there existed 13 antigenic types of ECHO viruses (Committee on the ECHO viruses, 1955); then six more antigenic types were chosen from this group (Committee on the Enteroviruses,

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1957). At present they number at least 24 antigenic types. Thus, 24 types of ECHO viruses, 24 types of Coxsackie and 3 types of poliomyelitis viruses form the family of human enteric viruses (Melnick, 1958).

As the investigations of the above mentioned and other workers (Kibrick et al., 1957; Neva, Enders. 1954; Rosen,1958, Honig et al., 1956, Gelfand et al., 1958) have shown, enteric viruses cause in people diseases with development of specific antibody. In addition to clinical forms, there exists a widely spread latent form of infection and also significant virus carriage of enteric viruses among population. Virus carriage is especially frequent among children, its incidence decreasing with the age. Similar to disease incidence, virus carriage has marked seasonal character.

This paper presents some data on the extent of dissemination and seasonal variations in isolation-rate of cytopathogenic enteric viruses from children of different children's institutions of Moscow.

Materials and methods

During 1957-1958 we examined 304 healthy children of 6 months to 8 years of age in five different children's institutions. The surveys were done in March-April, 1957, September-October, 1957, and May-June, 1958. During this period 654 stool specimens were collected from 304 children. It must be said that from this number 133 children were tested three times, 84 twice and 87 once.

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Stool suspensions were prepared by conventional methods.

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Virus isolation was made in monolayer trypsinized monkey kidney cultures. If no virus could be isolated on initial inoculation three blind passages were made.

Virus infectivity was determined in tissue cultures by inoculation of 0.1 ml 10-fold dilutions from 10^{-1} to 10^{-8} of virus-containing cultural fluid into each of 4 tube cultures per dilution.

For identification of virus isolates neutralization tests with 100 TCD_{50} of virus against homotypic immune sera to the three poliovirus types were used. Usually at least 40 units of antiserum were used. For identification of ECHO and Coxsackie viruses 20 units of antisera to 19 prototype ECHO viruses and 5 types of Coxsackie viruses (B1 - B5) were used. Each identification test with Coxsackie and ECHO antisera included control titrations of viruses to check the dose of the virus taken.

112 cytopathogenic enteric viruses were isolated from 654 stool specimens. In addition to polioviruses a large group of ECHO and Coxsackie viruses was isolated. Among 95 strains identified by now 15 strains belonged to polioviruses (16%), 41 to ECHO viruses (43%) and 39 to Coxsackie viruses (41%). The remaining 17 strains could not be typed by our collection of antisera.

Age distribution of the carriers of isolated viruses is presented in fig. 1. The study population consisted of children of 6 months to 3 years of age in nurseries, 3 to 7 years in two kindergartens and 7-8 years in the first grade of a boarding-school.

As is seen in fig. 1, most of the enteric viruses were

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isolated from children in the age-group of 1 to 5 years. Thus, 102 of a total of 112 isolates (91 per cent) were in the age-group of 1 to 5 years. The remaining 10 viruses were distributed in the following way: in the age-group under one year - 4 isolations (3.5%), in the age-group of 5 to 7 years - 6 isolations (5.3%). There were no virus carriers among school-children (7-8 years) of the boarding school surveyed. Similar age-distribution of virus carriers was observed in different periods of the survey. Of 55 viruses isolated in the first survey 40 were from the age-group of 1 to 5 years. All the 19 viruses isolated during the second survey were from the same age-group. And, finally, of 38 viruses isolated during the third survey 34 were again from children of 1 to 5 years. Thus, most extensive dissemination of enteric viruses was observed among nursery-age children and among younger groups of children in kindergartens.

Besides characteristic age-distribution of enteric virus isolates some seasonal variations in frequency of isolation were observed. As was mentioned above, the survey was carried out during the spring and autumn of 1957 and the summer 1958. From 297 children examined in the spring of 1957 55 enteric viruses (18.5%) were isolated. Type distribution of the isolates by periods of survey is shown in fig. 2.

Polioviruses and ECHO viruses were most prevalent in the spring of 1957. Of 11 poliovirus strains one belonged to type I and 10 to type III.

Among ECHO viruses most prevalent were type 6 and type 9 (20 strains) and also type 14 (6 strains). There was only one strain of ECHO-8.

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Coxsackie viruses were represented by two strains of Coxsackie B-5 virus.

From 216 children examined in the autumn of the same year 19 enteric viruses were isolated, which amounts to 8.7%, or two times less than in spring. In this period, as before, polioviruses and ECHO viruses again prevailed. But while in spring poliovirus isolates belonged mainly to type III, this time type I polioviruses were predominant (3 of 4 isolates).

Changes in type composition of virus isolates were observed among ECHO viruses as well. Of 14 strains identified as ECHO, 6 belonged to type 7, five to type 14, and, finally, there were strains of types 5, 12 and 19, one of each type.

In the late spring and early summer of 1958 141 persons were examined who yielded 38 viruses. This was 26.9% which was 3 times greater than isolation rate in autumn.

In this survey enteric viruses were represented by Coxsackie group of viruses exclusively. There were five Coxsackie B-2 strains and 32 Coxsackie B-3 strains.

Conclusions

1. In three observation periods of spring and fall, 1957, and spring and summer, 1958 112 cytopathogenic agents were isolated from 654 stool specimens of 304 healthy children. Of 95 identified strains 16 per cent were typed as polioviruses, 43 per cent belonged to ECHO group and 41 per cent to Coxsackie group of viruses.

2. Considerable increase in isolation-rate in summer-spring season and marked reduction in the middle of autumn was

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observed. Thus, in the spring of 1957 incidence of virus carriage among healthy children was 18.5 per cent whereas in the fall of the same year 8.7 per cent. In the spring-summer months of 1958 marked increase of virus carriage (26.9 per cent) was again observed in healthy children.

3. For reducing possible interference between vaccine strains of live poliovirus and enteroviruses latently circulating among population it is necessary, in choosing time for immunization programs, to take into consideration irregularities of virus carriage in different seasons and in different age-groups.

4. Long-range regular observations on changes in the dynamics of intestinal virus carriage in different age-groups living under various sanitary conditions should be continued.

References

1. Melnick, J., Rierdan, J., Curnen, E., Macrae, A. Fed. Proc., 1953, 12, 454.

2. Melnick, J. Am. J. Publ. Health., 1954, 44, 571.

3. Melnick, J., Ann. N.Y.Acad. Sci., 1955, 61, 754

4. Ramos-Alvarez, M., Sabin, A., Proc.Soc.Exp.Biol., 1954, 87, 655

5. Ramos-Alvarez, M., Sabin A., Am. J.Publ. Hlth., 1956, 46, 295

6. Hammon, W., Ludwig, E., Sather, G., Schrack, W., Ann. N.Y. Acad.Sci., 1955, 61, 979

7. Hammon, W., Ludwig, E., Sather, G., John, D., Am. J.Publ. Hlth., 1957, 47, 802.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

8. Hammon, W., Ludwig, E., Pavia, R., McCloskey, L., Sather,G., Ann. N.Y. Acad.Sci., 1957, 67, 304

9. Committee on the ECHO viruses, Science, 1955, 122, 3181,1187

10. Committee on the Enteroviruses, Am.J. Publ. Hlth., 1957, 47, 1156

11. Melnick, J., Progress in Medical Virology, 1958, 1, 59.

12. Kibrick, S., Melendez L., Enders J., Ann. N.Y. Acad. Sci., 1957, 67, 311

13. Neva, F., Enders, J., J. Immunol., 1954, 72, 304.

14. Rosen, L., in: Abstracts of the Papers, Sixth international congr. on tropical Med. & Malar., Lissabon, 1958.

15. Gelfand, H., Henigst, W., Fox, J., Le Blanc, D., Ibid.

16. Honig, E., Melnick, J., Isacson, P., Parr, R., Myers, J., Walton, M., J. Exp. Med., 1956, 103, 247.

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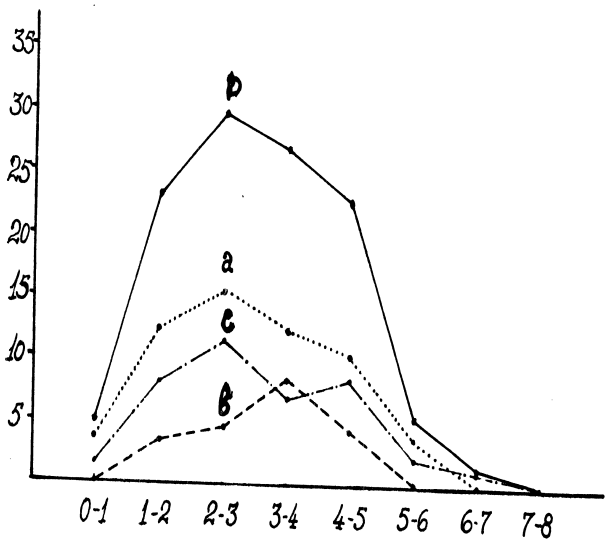

Fig. 1 - Number of enteric virus isolates by agegroups

a - first observation period (March-April, 1957)

b - second observation period (September-October, 1957)

c - third observation period (May-June, 1958)

d - total

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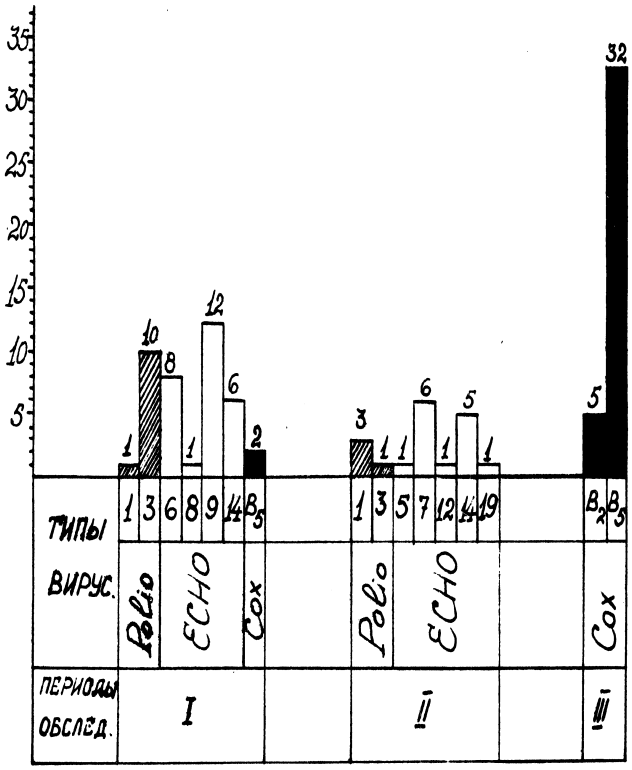

Fig. 2 - Quantitative distribution of types of enteric virus isolates by observation periods

I - March - April, 1957

II - September - October, 1957

III - May-June, 1958.

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ON LATENT IMMUNIZATION OF HEALTHY CHILDREN IN MOSCOW WITH NATURALLY OCCURRING (WILD) POLIOMYELITIS VIRUSES

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Observations on clinical manifestations of poliomyelitis have revealed most different variations from silent and non-paralytic forms to different extent of classical paralysis. During epidemies paralytic cases with severe involvement prevail. Therefore until recently attention of scientists was concentrated mainly on studies of regularities of epidemies associated with peculiar epidemic spread of poliomyelitis. As Melnick (1957) stated, however, epidemic outbreaks of poliomyelitis could not serve a model for correct understanding of natural distribution of polioviruses. Apparently these were the reasons for which long-range studies and observations of healthy children population without recognized clinical cases of poliomyelitis were started almost simultaneously in several largest laboratories (Gelfand et al., 1957; Fox et al., 1955, 1956, 1957; Honig et al., 1956; Hammon et al., 1955; Melnick et al., 1957, Isaacson et al., 1957).

These investigations consisted in monthly tests of stool specimens and examination of blood specimens collected twice yearly.

General conclusions of these observations showed that under natural conditions polioviruses are widely spread in the environment. Their dissemination is favoured by overcrowded living conditions, long family contacts and absence of immunity to poliomyelitis in certain population groups.

In this connection the highest incidence of latent infection was found among children population.

Antibody titers which to a certain extent determine relative resistance to paralytic poliomyelitis were found to be

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much greater in younger age-groups than in adults. Adults are rarely involved by the process of natural infection and this explains the absence of homologous antibody. Cases of reinfection were observed among immune persons, and marked increase in antibody titers was more frequent among children than among adults.

As the investigations of the above authors showed, dissemination of poliomyelitis viruses occurs all the year round but the incidence of subclinical infections is somewhat higher in summer-fall periods. Incidence of infection with type I and type III polioviruses varied in different observation periods whereas incidence of infection with type II poliovirus was more or less uniform.

We investigated incidence of poliomyelitis antibody in children who were regularly examined for enteric virus carriage.

Materials and Methods

Serum and stool specimens were collected from healthy children of three institutions representing different age-groups (nursery, kindergarten, 1st grade of boarding-school) during spring and fall, 1957.

Finger blood was collected into a graduated pipette in 0.8 ml. amounts and diluted with physiological saline 1:5.

Neutralizing antibodies against 100 TCD_{50} of strains "Lugovskoy", "Ovchinnikov" and Leon were determined by cytopathogenic neutralization test in trypsinized monkey kidney cell cultures. Each serum dilution (1:10, 1:50, 1:250) was

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tested in two tissue cultures.

During 1957 we collected 130 paired and 17 single serum specimen from 147 children, so we tested a total of 277 specimens.

For virologic investigations we collected stool specimens from children in the same institutions. From 218 children 389 stool specimens were collected, of them 218 specimens in March-April and 161 specimens in September-October. Isolation and identification of enteric cytopathogenic viruses was carried out by conventional methods.

Results

During the observation period from 218 children in the age of 1 to 8 years 10 poliovirus strains (4.5%) were isolated, of them 7 belonging to type III and 3 to type I. All type III strains were isolated from children under 3 years (nursery No. 397), from stool specimens collected in March, 1957.

Type I polioviruses were isolated from stool specimens collected in September-October, one of these strains was isolated from a child of 2.5 years old (nursery No. 397), and two strains from two siblings going to kindergarten No. 409. No polioviruses could be isolated from children of the boarding-school.

Examination of serum specimen collected in April 1957 showed that of 147 children only 11 (7.4%) possessed no neutralizing antibody to any one of the three poliovirus types (in 1:10 dilution).

In 53 serum specimens (36%) neutralizing antibodies to all the three types of poliovirus were found, in 56 specimens

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(38%) to two poliovirus types and in 27 specimens (18.3%) to only one type.

Examination of second blood specimens demonstrated increase in the number of children possessing neutralizing antibody to one virus type (25%). No significant change was shown in the number possessing antibody to two and three virus types. Only 3.3 per cent of 130 children examined had no neutralizing antibody in 1:10 dilution of serum (fig.1).

Relationship between the age of children and per cent of children with antibody to one or more poliovirus types is shown graphically in fig. 2.

Age-group of 1 to 3 years was represented by children from nursery No. 397 where 9 months previously four children had been hospitalized on epidemic indications for poliomyelitis. Serum specimens from three of these children neutralized type III poliovirus in 1:250 dilution. 70 per cent of children from this community possessed type III neutralizing antibody in serum dilution 1:50 and higher, and only 8 per cent of children (3 of 37) had no type III antibody (fig. 3a).

It should be said that in the interval between the two observations there were no dynamic changes in levels of type III antibody. More extensive dissemination of type III polioviruses in this community in the early spring of 1957 may be supposed to be the final stage of continued latent infection which could be caused by children returning from the hospital to the community.

As is seen in fig. 3, incidence of antibody to type I

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poliovirus was as high as that to type III. However, considering that type I virus was isolated from stool specimens collected in the fall, and that is 5 of 30 children dynamic changes in type I antibody titers were observed (not less than 5-fold decrease in titer), we may suppose that spread of type I poliovirus occurred in the period between two surveys (late spring - fall, 1957).

There was no virologic evidence of type II poliovirus dissemination. In 10 serum specimens, however, at least 5-fold increase of neutralizing antibody titer was observed. Apparently, latent infection with type II virus occurred in this community though perhaps less extensive than with type I and type III polioviruses.

The age-group of 3 to 6 years was represented by children from kindergarten No. 409. In first serum specimens collected from these children there was no significant difference between neutralizing antibody levels to the three types of poliovirus. Most of the sera examined contained antibody in dilutions 1:10 or higher. In second specimens, however, there were considerable changes both in neutralizing antibody levels and in prevalence of individual poliovirus types. On virologic investigation of these children type I poliovirus was isolated. As could be expected, 30 per cent of 81 children hat at least 5-fold increase in antibody titers. 49.3 per cent of sera tested contained type I poliovirus antibody in 1:50 dilution.

Considerable changes occurred in type III antibody levels. Number of children without antibody in serum dilution 1:10

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decreased with crrresponding increase in number of children possessing antibody at higher levels (1:50 and higher). At least 5-fold rise in antibody titers was observed in 25.9 per cent of sera.

As for type II antibody, there was a marked increase in the number of sera containing higher antibody titers and a slight decrease in the number of sera with low antibody levels. Despite such seemingly insignificant changes, in 11 cases there was rise of type II antibody titers (fig. 3b).

Somewhat different picture was observed in the next age-group, 7-8 years, which was represented by schoolchildren from a boarding-school. This group was not very numerous, and paired sera were collected only from 19 persons. Therefore percentage calculations here are not very significant. In the first examination 3.4 per cent of sera contained no poliovirus neutralizing antibody in 1:10 dilution, whereas all second samples had antibody at least to one poliovirus type (fig. 2b).

Antibody levels to types I and III polioviruses were low both in first and second serum specimens. Almost half of the sera (14 and 11 of 29, respectively) contained antibody in 1:10 dilution. Moderate and high antibody levels were present in most specimens from those children who had left the school by the time of the second survey.

As for type II antibody, about half of the specimens (14 of 29) contained antibody in 1:50 and 1:240 dilutions. Similar results were obtained with second sera specimens. Apparently prior to and during the survey type II polioviruses were more widely disseminated among these children.

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At least 5-fold rise in antibody titers to all three types of poliovirus was observed, in three sera to type I, in four to type II and in three to type III.

The data obtained indicate dissemination of three types of polioviruses among healthy children. Based on serologic data incidence of spread of each of the three types may be supposed to vary in different periods of observation and in different communities.

Sera which did not neutralize the homologous virus in 1:10 dilution were considered negative. Therefore serologic changes in antibody levels, with first serum negative, were causally related to primary infection with the corresponding virus.

But if any change in the antibody levels occurred in those cases where homologous antibody were present in 1:10 dilution such cases were considered to be reinfection.

Thus, in 130 paired serum specimens primary infection was observed in 29 cases, of them 10 with type I, 11 with type II and 8 with type III poliovirus.

Reinfection was observed in 53 cases, of them in 23 with type I, 13 with type II and 17 with type III. Of 53 cases of reinfection low antibody levels in first serum specimens (1:10) were found in 40 cases, and moderate levels (1:50) in 13 cases. Thus, with low antibody levels susceptibility to reinfection with homologous virus was 3 times higher than with greater antibody levels.

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Conclusions

Investigation of the dynamics of antibody response to polioviruses in healthy children as a result of latent infection with naturally occurring (wild) polioviruses will help to understand the mechanism of immunity development as a result of asymptomatic infection, including oral immunization with live poliovirus vaccine.

References

1. Malnick J., Walton, M., Isacson, P., Cardwell, W.,
Am. J. Hyg., 1957, 65, 1, 1-28.

2. Gelfand, H., Le Blanc, D., Fox, J., Conwell, D.
Am. J. Hyg., 1957, 65, 3, 367-389.

3. Fox, J., Gelfand, H., Bhatt, P., Le Blanc, D., Conwell, D.
Ann. N.Y. Acad.Sci., 1955, 65, 968-978.

4. Fox, J., Gelfand, H., Le Blanc, D., Conwell D.
Am. J.Publ.Hlth., 1956, 46, 3, 283-294.

5. Fox, J., Gelfand, H., Le Blanc D., Conwell, D.
Am. J.Hyg., 1957, 65, 3, 344-366.

6. Honig, E., Melnick, J., Isacson, P., Parr, R., Myers,J.,
Walton, M.
J.Exp. Med., 1956, 103, 2, 247-262

7. Hammon, W., Ludwig, E., Sather, G., Schrack, W.
Ann. N.Y. Acad. Sci., 1955, 61, 979-988

8. Isacson, P., Melnick, J., Walton, M.
Am. J. Hyg., 1957, 65, 1, 29-42.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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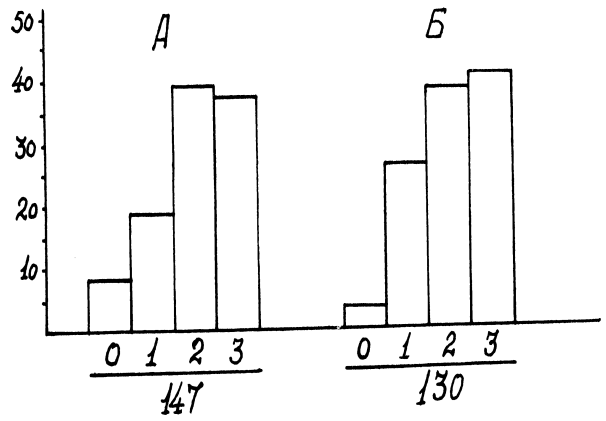

Рис 1.

Fig. 1 - Presence of neutralizing antibody in healthy children (per cent). Serum dilution 1:10

Legends

A - first blood specimens

B - second blood specimens

Numerator: 0 - absence of antibody

1.- Antibody to one virus type

2.- Antibody to two virus types

3.- Antibody to three virus types

Denominator - number of children tested.

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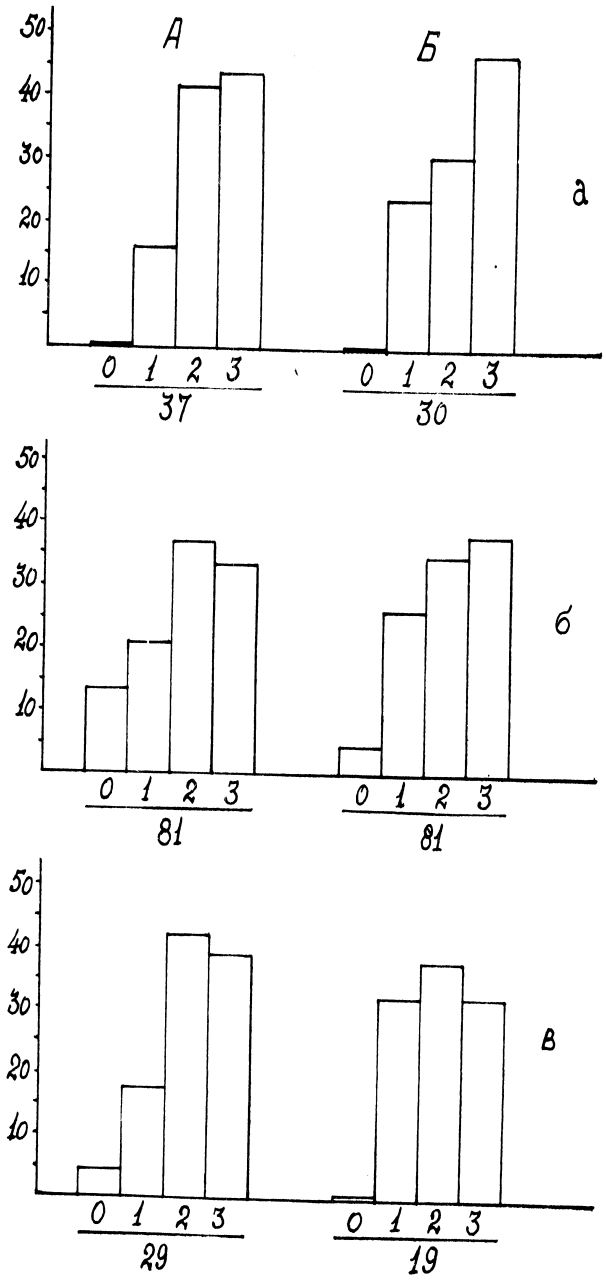

Fig. 2. - Per cent distribution of neutralizing antibody in healthy children by ages. Serum dilution 1:10.

a - 1 to 3 years

b - 3 to 6 years

c - 7 to 9 years

Legends same as in fig. 1

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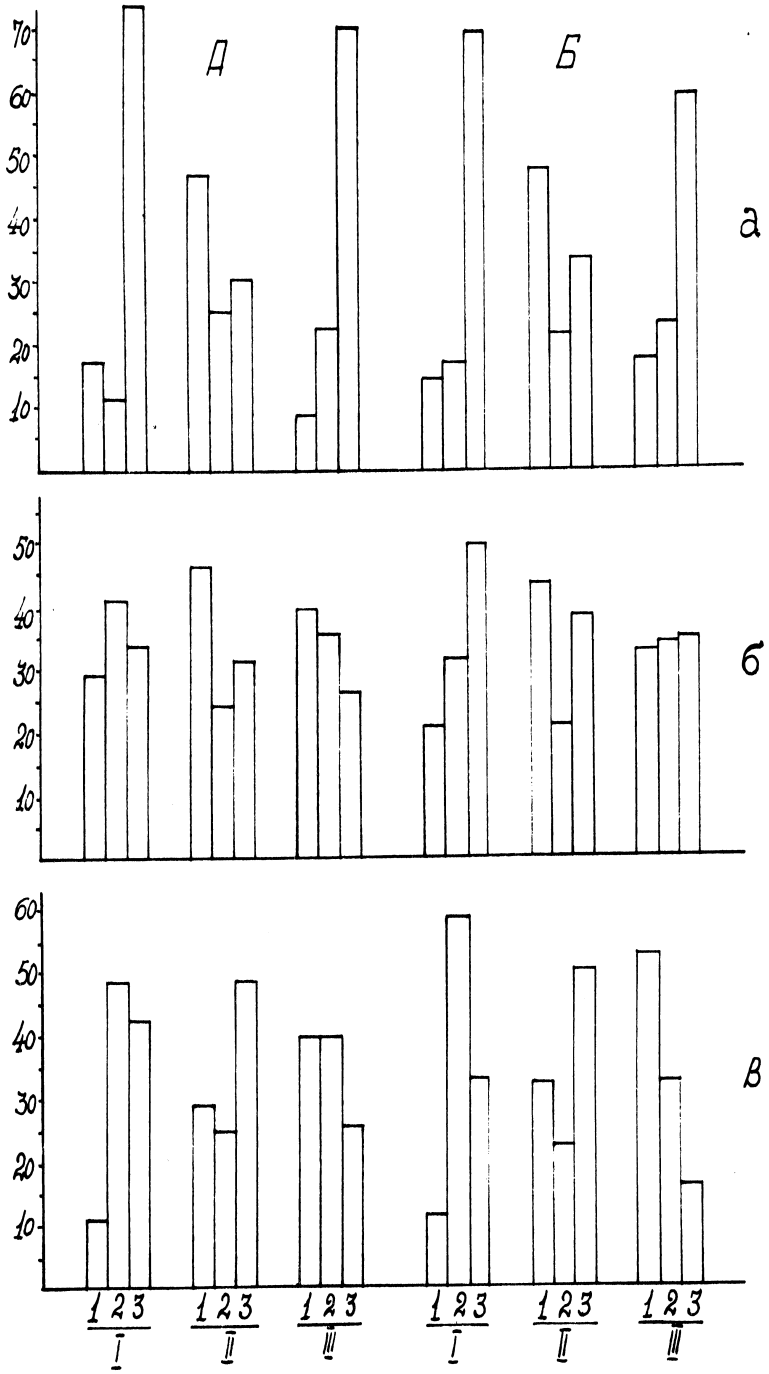

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Fig. 3. - Levels of neutralizing antibody by ages of children and poliovirus types.

Nominator - 1, 2, 3 serum dilutions below 1:10, 1:10 and 1:50 and higher

Denominator - poliovirus types.

Legends same as in fig. 2.

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MATERIALS ON IMMUNOLOGICAL AND EPIDEMIOLOGICAL EFFICACY OF LIVE VACCINE AGAINST POLIOMYELITIS

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The large=scale use in recent years of Salk killed vaccine to control poliomyelitis has not eliminated the threat of acute anterior poliomyelitis developing in triply incoculated children and has failed to influence the virus circulation in childrens' establishments. Restricted duration of the post=vaccinal immunity required repeated immunization following a completed cycle of triple inoculations with the killed vaccine.

The necessity to sacrifice vast numbers of monkeys to prepare each and every million doses of killed vaccine has already become a source of considerable difficulties in securing the needed stock of monkeys for the ever=increasing production of this preparation.

At present the large=scale output of a complex, costly and insufficiently effective Salk vaccine, which necessitates inflicting additional traumas to children by repeated injections, can be entirely dispensed with in view of the possible complete replacement of the killed vaccine with a more effective, fully harmless, maximally convenient and accessible live one, administered perorally and prepared from the A.Sabin or G.Koprovsky strains /13/.

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The live vaccine is devoid of principal defects specific to that of Salk. It is not only capable of producing a lasting humoral immunity, which precludes viral invasion into the central nervous system, but tends also to make the intestinal tract highly insusceptible, this ruling out the development of the causative agent in a receptive organism. The live vaccine is the groundstone for future solution of a major epidemiological task- that of limiting and eradicating a vast ocean of highly pathogenous "wild" viruses, tightly surrounding our adolescent population- an undertaking entirely outside the scope of the killed vaccine.

It was thanks to the investigations of our laboratory, effected in 1956-1958, that the broad study into the epidemiological effectivity of live vaccine against poliomyelitis, obtained from the A.Sabin's strains, could be organized. This was effected in the USSR during 1959 by the Institutes of Experimental Medicine and Poliomyelitis of the AMS of the USSR and covered 3 million children, vaccinated in the period of April-May, prior to the seasonal upsurge of the disease. In those years we had assumed great resposibility in testing the innocuousness and immunogenic properties of the Sabin's vaccinal strains on progressively increasing numbers of children belonging to junior age groups, which, by the end of 1958, permitted us to give positive answear as to the innocuous nature and efficacy of live vaccine, this having been the basic point of our reaearch. The positive solution of the problem rested on the data of the laboratory and clinical examination covering 2500 healthy children of the creche and pre=school age groups, immunized with live vaccine preparaed in Leningrad /15/.

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The results of this work, carried out in close contact with the clinic for nervous diseases of the Leningrad medical pediatric institute (E.F.Davidenko) and Infectious clinic of the Leningrad Sanitary=Hygienic Medical Institute (V.V. Kosmachevsky) proved complete harmlessness of the live vaccine, both to the vaccinated children and to susceptible groups of non=vaccinated adolescents immediately contacting the latter.

Observations carried out for a space of two years and covering both the inoculated and non=inoculated children bore out that the live vaccine did not produce any leasions of the central nervous system, reproducible of even the mildest forms of meningeal poliomyelitis, failed to affect the intestinal tract, respirative tract or any other organs. In those inoculated with live vaccine even the temperature reaction was of a very rare occasion and its frequency was similar to that encountered in analogous establishments for children, where live vaccine was not introduced at all. (2,5,11).

Observations have established high immunogenous activity of live attenuated vaccine for susceptible children, provided its repeated administration was in the form of monovalent vaccines. A somewhat lower activity was achieved by a single introduction of two or three viruses of different types in a combined divaccine or trivaccine.

A consecutive triple immunization of susceptible children with monovalent preparations of live vaccine against poliomyelitis of the I,II and III types ensures obtaining of comparable indices for a quantitative rise in the number of antibodies, irrespective of the order in which alternate individual serotypes of the vaccine. It has been noted that the indices showing the antibody rise against the virus of the III type are regularly behind those of humoral immunity with

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respect to the I and II types (12).

The groups of susceptible children who responded by development of humoral immunity to a single introduction of monovalent vaccines comprise 90-95% for the vaccines of the I and II types and around 80-90% for those of the III type. Revaccination of triply inoculated children with the polyvalent vaccine of the I,II and III types corrects the shortcomings of the first round of immunization and imparts complete immunity to the greatest part of refractory children.

The prepared polyvalent vaccine containing 100 000 of tissue cytopathogenic units of each virus type represents a most appropriate form of universal preparation adaptable for practical use.

Single administration of trivaccine stimulates a somewhat lower level of antibodies to all three types, as compared with the triple introduction of a monovalent vaccine or divaccine, but twofold and, particularly, triple administration of trivaccine ensures immunological changes approaching a 100% level.

Exceptionally convenient, speedy and effective is triple immunization effected along the following scheme: monovaccine of the I type, divaccine of the II and III types, all of these conducted with an interval of 1 month. This scheme secures maximal immunological efficacy and requires the same amount of the preparation as the triple introduction of monovaccines, with subsequent revaccination in 1-3 months. Its merit lies in the rapid completion of the entire immunization cycle, without encumbering the medical staff with the performance of the fourth revaccination.

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The high immunogenous effect of live vaccine is associated with the propagation of vaccianl viruses in the intestinal canal of inoculated children, which follows a rigid cyclic pattern with the maximum accumulation of the virus between the 7-21 days and subsequent gradual decline in its concentration during the further 15-20 days.

The multiplication of the virus is of a highly regular character, provided there is not interference with other viruses, and it reaches its maximal intensity in children with a low level of immunity to poliomyelitis, while in subjects whose blood comprises specific antibodies- it tends to show a progressive decline.

The major feature peculiar to the live vaccine was the fact that it helped to form intensive and prolonged resistance of the intestinal tract to repeated introduction of maximal doses of homologous viruses, whereby these fail to propagate and are swiftly eliminated from the intestinal canal/4/.

On rare occasions the repeatedly administered virus displays its ability to multiply, but the intensity of this process is by far inferior to the initial propagation intensity of the virus in the same child.

Long-term observations of the intestinal canal immunity in children inoculated for a period of 4-24 months by live vaccine have demonstrated that their revaccination at the above dates, following the first inoculation, tends to confirm the maintainance of an intensive and regular immunity of the intestinal canal to the repeated infection with the vaccinal strain.

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The resistance of the intestinal tract in children to the primary introduction of vaccinal strains stands in direct relationship with the state of their humoral immunity to the homologous virus. With low initital titres of virus=neutralizing antibodies / 1:4-1:16/ the intestinal tract was noted to possess poor resistance to its invasion with vaccinal strains. On the other hand, with elevated titres of antibodies there is either no propagation of vaccinal strains at all, or they develop slowly within a very short space of time.

To secure lasting and intensive resistance / local/ of the intestinal tract, of importance is garanteed inoculation with a high=quality vaccine, in view of unreliable results of immunization developing after contacts with non=vaccinated children.

In the main, the results of vaccination are dependent upon the dose of the preparation actually introduced, and also on the state of specific and non=specific immunity of the children subject to inoculation.

Liquid vaccine comprising $10^{7.0}$ -$10^{7.5}$ TCU_{50} of the vaccine represents a garanteed preparation for peroral immunization against poliomyelitis, which ensures maximal uniformity and standard dosage for individual children.

Intensive discharge of vaccinal strains from the intestine of vaccinated children, occurring during the first month after immunization, produces natural dissemination of the vaccinal virus among susceptible subjects, coming in contact with the vaccinated ones/8/.

This process of the vaccinal virus extending and covering the contact groups is one of the most characteristic features of the live vaccine against poliomyelitis, creating conditions

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favorable for involving into the immunization process of those who come in contact with the immunized groups of the population, and also producing possibilities for revaccination of those already inoculated.

There should be, however, no overestimation of the factual epidemiological significance of such a " blind" immunization. Thus, for example, the enclosed herewith materials, obtained in 1959 as a result of epidemiological observations covering Bielorussian and Moldav republics were indicative of the fact, that non-vaccinated groups of children who were in potential contact with the vaccinated ones showed a fairly high incidence of acute anterior poliomyelitis, differing very little from the morbidity rate registered for the population sections with no actual contacts with the vaccinated.

"Blind" infection with vaccinal virus reaches its maximal intensity among children in the junior age bracket, for instance, in creches. With the increasing age of children the indices for contact infection show a rapid decline of intensity (children of pre-school and, particularly, school age/, so that in susceptible adults the indices for the contact spread of vaccinal virus are minimal.

Great attention was paid by us to the cardinal question of possible reversion of Sabin's vaccinal strains to their initial pathogenic variant, following frequent and prolonged passages via the intestinal tract of susceptible children/15,16/.

The study of changes in the neurotropic activity of vaccinal strains in monkeys, following prolonged artificial or natural passages through susceptible children, revealed the appearance of periodic and relatively slight intensification of

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neurotropic properties in vaccinal strains, which,however, did not lead to a progressive rise in their neurovirulence.

These data of ours were , in a large measure, responsible for putting an end to a very pointed discussion on the dangers connected with the reversion of the vaccinal strains group investigated by us.

The data confirming the innocuous nature of the vaccine made it possible for the Commission on Sera and Vaccines and the Board of the Ministry of Public Health of the USSR to permit in November 1958 to undertake large-scale epidemiologic observations with the view of investigating the harmlessness of the live poliomyelitic vaccine.

In April and May 1959 we utilized the stocks of live vaccine at the disposal of the Virusology Department of AMS Institute of Experimental Medicine, amounting to about 2.000 0000 doses for immunization of 1.700 000 adolescents aged up to 14-18 years in Bielorussian, Latvian and Moldavian republics,while in June-July 1959 we carried out similar vaccinations in Pskov and Novgorod regions with the vaccine obtained from the AMS USSR Institute for the Study of Poliomyelitis. The vaccination was effected twice: the first / in April 1959/ with the monovaccine of the I type, and the second /in May 1959/- with divaccine of the II and III types.

BASIC PRINCIPLES UNDERLYING THE ORGANIZATION OF VACCINATIONS AND THE STUDY OF EPIDEMIOLOGICAL EFFECTIVITY OF THE LIVE VACCINE

The Ministries of the Union Republics responsible for the vaccinations made arrangements in advance to instruct in detail the chief physicians and epidemiologists of the district

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sanitary=epidemiological stations about the tasks and procedures of vaccination and, together with them, compiled a detailed schedule of vaccinations and drew up personal lists of vaccination teams at a rate of 300-500 vaccinations per day for 1 team, including one physician / feldsher/ and 2 qualified nurses.

Analogous work was performed in every city or district, with all members of the medical staff participating in the immunization summoned up to receive appropriate instructions.

Official institutions responsible for the vaccination sent their permanent representatives to each city or district, who were to stay there for the whole period of immunization and assist in its proper execution.

Prior to vaccination and during its performance there was organized large=scale health=educational work with the view of familiarizing parents and administration of childrens' establishments with the tasks and importance of vaccination.

In organized bodies of children vaccination was done right on the spot. Children not attending such establishments were vaccinated at childrens' polyclinics covering respective residential areas, or during house to house visits.

All vaccinated children and also non=vaccinated ones, who for different reasons were dispensed from immunization, were registered by the vaccination teams with their names entered either into special lists or put on individual unified forms, compiled separately for each childrens' establishment or residential area. The lists were to contain basic information on the vaccinated and the data on preceding vaccinations against poliomyelitis.

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The district epidemiologist summed up in a standard report on vaccinations all records relative to their actual performance, according to individual establishments or villages. A copy of this report was sent to the regional sanitary-epidemiological station or to the local institute of epidemiology and microbiology, which generalized the results of each vaccination.

To study the poliomyelitis incidence in 1959 and epidemiological efficacy of vaccination against poliomyelitis a scientific group was set up in each republic, including clinicians and epidemiologists, appointed by a special order of the Ministry. The task of these groups was an expert investigation of each notified poliomyelitis case within the areas covered by vaccination and deciding on diagnosis in questionable or controversial instances.

In order to study the epidemiological efficacy of active immunization against poliomyelitis two control groups were placed under observation on the territory of each republic or region. The first of them included non-vaccinated children standing in direct or potential contact with the vaccinated ones on the territory covered by immunization with live vaccine/ internal control/. The second control group comprised children and adolescents at the age of up to 14-18 years, residing in areas not covered by the immunization with live vaccine /external control/.

In selecting groups to be immunized with live vaccine it was recommended to cover territories with maximal poliomyelitis incidence in the past years, leaving areas with a lower morbidity rate to serve as external controls.

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The vaccination coverage did not exceed 50-75% of the population figure for districts subject to immunization.

To arrive at a well-grounded evaluation of the epidemiological efficiency of the live vaccine we endevoured to safeguard the following conditions:

1. Securing comprehensive information on the incidence of the disease in all three groups of vaccinated and non-vaccinated population. The following special measures were undertaken to assure complete detection of all cases of acute anterior and non-paralytic variants of poliomyelitis:

1. Right from the start of vaccinations a system of urgent notifications was introduced by an order of the Ministry of the union republic, covering each case diagnosed as poliomyelitis in any part of the republic or region.

These notifications, including brief information on the diseased, were transmitted either by telephone or wired to the local republican sanitary-epidemiological station or to the institute of epidemiology and microbiology.

2. From among the organized groups of travelling neuropathologists a specialist would be urgently sent to the pertinent area, to verify the diagnosis and collect basic materials for virusological and laboratory investigations (feces of the diseased and first venous blood test. The second blood test was made 3-4 weeks following the onset of the disease.)

3. The poliomyelitis patients were hospitalized in central in-patient departments of regional and republican hospitals, immediately upon the onset of the disease, and when this was impossible,- after termination of the acute period of the disease. Experienced neuropathologists made accurate diagnosis in each individual case, or verified the correctness of the primary clininical diagnosis, with due consideration of laboratory

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investigations.

4. In order to analyse the epidemiological effectivity the figures for recorded cases were used separately according to groups of acute anterior and non-paralytic variants of poliomyelitis. Beside the acute anterior form the group of paralytic poliomyelitis also included the more authentic variants of spinal and bulbo-spinal affections with residual manifestations. The pontine variants, among which predominant were affections of non-poliomyelitic nature, were included in the group of non-paralytic poliomyelitis.

5. The analysis of the epidemiological effectivity rested upon the data of the incidence rate, recorded during the whole period of the epidemiological rise in the intensity of the disease, covering no less than 6 months of observations. The processing of the materials relative to the efficacy of vaccinations was timed so as to encompass the period of June-December 1959, which commenced 3-4- weeks after completion of the second immunization.

II. As a quality index for recording of epidemiological effectivity of vaccination served the scope of laboratory investigations covering registered cases of the disease, including comprehensive feces examination in majority of patients figuring under the diagnosis of poliomyelitis. It was recommended that the materials should be obtained not later than on the 10th day upon the onset of the disease, repeated collection of feces be made in the first days of the affection, with their investigation performed separately, or after after combination of all specimens.

In addition to virusological examinations of feces, which

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demonstrated excretion of poliomyelitis virus of the I type in 50% of the examined and those of the II and III types - in 15%, we also conducted serological investigations of the patients.

In instances of dubious clinical diagnosis positive laboratory data permitted it to include such patients in the poliomyelitis group. Investigated cases with negative laboratory data, but positive clinical diagnosis were also considered as poliomyelitis.

III. A very important pre=requisite for the performance of epidemiological analysis relative to the efficacy of vaccinations was the availability of accurate information on the numerical age=composition within the categories of children and adolescents covered by immunization with live vaccine and included in the groups of internal and external controls/Table I/.

The local statistical agencies furnished information on the age=distribution of the population inside the territories covered and not covered by vaccinations for all of the above=cited groups.

During vaccinations measures were taken to secure accurate registration of immunised children by using either individual forms or registration lists, with the primary analysis of the age=distribution among the vaccinated at the district sanitary=epidemiological stations.

The above information, compiled in a standard form, was summed up by the sanitary=epidemiological stations or by the epidemiological department of the Institute of epidemiology and microbiology.

If in the given republic or region there happened to be a fairly large group of children covered by triple immunization

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with the killed Salk vaccine we abstained from immunizing them with the live vaccine, but put them on record as a separate group, which would provide us the solution of the question as to the comparative efficacy of the live and killed vaccine under comparable epidemiological conditions.

DISTRIBUTION OF VACCINATED AND CONTROL GROUPS IN DIFFERENT REPUBLICS

In the Bielorussian republic a total of 542 519 children were encompassed by the immunization. They were urban inhabitants with the age of up to 14 years. Numerically this meant 63% of the entire urban population of under-aged. The remaining 37% of children / 315 336/ constituted a group of internal control. The children of rural districts, whose number exceeded that of the urban ones in the same age bracket by 2.5 times, were not subject to immunization with live vaccine and they constituted the group of external control. In the past years the absolute number of poliomyelitis cases among children of the rural and urban groups was approximately equal, this being due to a relatively lower poliomyelitis incidence rate in rural areas during the past years. /10/.

In the Moldavian SSR vaccinations covered 13 central districts of the republic and 4 large cities situated in the midst of them, whose inhabitants make up somewhat over one half of the entire population of the republic. In previous years this territory accounted for about 50% of poliomyelitis morbidity. The total number of vaccinated children and adolescents comprised 407 530 in the age group ranging from 9 months to 18 years. 156 531 subjects were in the group of internal control and 482 430, within the same age bracket, constituted external controls (1).

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In the Latvian SSR the vaccinated children and adults numbered 400 000. They came from Riga and from a number of other districts of the republic and their maximal age was 30 years (3).

Somewhat later, in June and July, the object of immunization were the cities and villages of Novgorod and Pskov regions, were it embraced about 400 000 children with the age of up to 14 years, the proportion of non=vaccinated children in the same age bracket amounting to 20%. (4).

In all republics vaccinations were performed twice, with an interval of 1 month; the first immunization with the vaccine of the I type was made in April, the second, with divaccine of the II and III types - in May 1959. The study of the epidemiological effectivity of vaccinations was started from June 1 1959 i.e.- 2 weeks after termination of the second immunization and 1 1/2 months following completion of the first immunization.

THE STUDY OF THE IMMUNOLOGICAL PATTERN OF THE POPULATION BEFORE AND AFTER VACCINATION.

It is well known how important are humoral indices of the blood in children and adults for the epidemiological prognosis of poliomyelitis and for well=substantiated assessment of the immunization results.

When commencing immunization with live vaccine we made preliminary determinations of the proportion of subjects susceptible to poliomyelitis within different age groups of the population undergoing vaccination with respect to various serotypes of the vaccine. . To do this, the sera of population groups under examination, taken prior to vaccination, were made subject to color test in a dilution of 1:4, together with 100 cytopathogenic doses of the virus and renal cells of

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monkeys (L.M.Kurnosova and G.P.Zhilova).

By unsing material derived from over 2500 examined sera it could be established that in different geographical zones of the USSR there exists a fairly large stratum of susceptible children, whose proportion attains the maximal figure for the age=bracket of 2-4 years (60% and above) and then gradually goes down as the age increses up to 16-20 years (Table 2).

Parallel investigations of all negative sera in the reaction of cytopathogenic activity neutralization in monostratal tissue cultures indicated the need for diminishing the color test index by 25-30%. In consideration of the fact that a similar correction is required also for the sera of those examined with color test after vaccination, we - we decided to adopt the percentage of negative sera as a conventional index of factual susceptibility.

The evaluation of the susceptible subjects made on the basis of calculated indices showing the percentage of negative sera testify to the fact that over 25% of the population comprising the districts under examination were susceptible to one of the poliomyelitis virus serotypes, while 10-15% were among those maximally susceptible / triply negative/. Table 3 presents an example of such evaluation for the vaccinated inhabitants of the Moldavian SSR.

With the proportion of susceptible children amounting to 25% out of the total of 1 700 000 vaccinated we had no less than 400 000 subjects susceptible to the virus of the I,II and III types and over 100 000 triply negative children. It is to be noted that, in spite of the fact that hundreds thousands of

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children were given sumultaneously a highly active vaccinal - virus, which thereby joined in the intensive circulation among the contact children, we not only failed to observe any rise- in the poliomyelitis incidence during the first months following immunization on the territories covered by vaccinations, but , quite the contrary,could mark a distinct decline of the polio- myelitis morbidity, when compared with the anticipated indices, figured out on the basis of the disease incidence among external controls, where no live vaccine had been introduced.

The twofold immunization carried out in April and May 1959 has brought substantial changes into the immunological pattern of the population by curtailing the percentage of sus- ceptible children and adolescents to 1/4-1/8 of the original figure /Tables 4,5,6/.

The third immunization, completed in a number of places and effected with the trivaccine containing 100 000 cytopatho- genic doses of each type, called forth additional and very sub- stantial changes in the numerical level of antibodies, thereby reducing the proportion of susceptible population within the groups of children exposed most to the hazards of the infection / age=bracket 0-4 years/ down to 2-5%.

The above results testify to a high immunological efficacy of the live vaccine employed in triple immunization with the monovaccine of the I type, divaccine of the II and III types and trivaccine of the I+II and III types, which tends to almost entirely eliminate the susceptibility among the population, and protects it against all of the three virus serotypes.

THE EFFECT OF VACCINATION ON THE SEASONAL DYNAMICS OF POLIOMYELITIS AND ITS INCIDENCE RATE

Of high significance is the dynamics of paralytic polio- myelitis cases in the Bielorussian,Latvian and Moldavian repub-

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lics , as well as in the Novgorod and Pskov regions of the Russian Federation. There,among the massively vaccinated population, for the first time in recent years noteworthy was almost complete absence of the seasonal incidence rise in June-October, which had been a regular feature for these areas. This observation could be also confirmed in the instance of contact groups of non=vaccinated children (internal control) , whose numbers sharply decreased on the territories covered by immunization in connection with the vaccination of a large proportion of under=aged population. Radical changes in the usual for these areas seasonal dynamics of poliomyelitis serves as a convincing illustration for the effectivity of the live vaccine. (Table 7).

This can be demonstrated in a most clear=cut fashion by the data showing the distribution of paralytic poliomyelitis cases, registered during the period subsequent to vaccination, i.e. June=December 1959, among children of different age=groups vaccinated and non=vaccinated with live vaccine in different republics (Table 8).

Particularly demonstrable results in favour of the efficacy of live vaccine were obtained during May-December in the Bielorussian SSR. Among the total of 74 868 children aged up to 3 years and inoculated with live vaccine during the months of May-December 1959 on records were only two cases of paralytic poliomyelitis. At the same time, among 77 612 non=vaccinated children of the same age, who were in potential contact with the immunized ones, the number of paralytic cases amounted to 35. This means a reduction in the incidence of the disease among vaccinated 17.5 times over and above the anticipated figure, and with respect to the morbidity rate among external controls- 8.5 times over that level.

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The efficacy of live vaccine in senior groups of pre=school and school ages is represented by an index equal to 2-3, this being due to a low poliomyelitis incidence rate in respective control groups (4.0 per 100 000 for children of 7-14 age bracket) The summary morbidity index for the whole group of vaccinated comprised 1,6 per 100 000,22.0 per 100 000 for internal control and 9.0 per 100 000 for external control / Table 9/.

In the Moldavaian SSR 2 cases of paralytic poliomyelitis were registered for a total of 354 607 vaccinated children aged up to 14 years. In the group of internal control which numbered 88 853 subjects, i.e. 1/3 of the vaccinated group on records were 7 instances of paralytic poliomyelitis, this signifying a fall in the incidence of the disease by over 8 times. As contrasted with non=vaccinated groups of external control, where altogether 41 cases of the disease came upin a total of 310 809 children, or 22.5 per 100 000, the decline in the morbidity rate is as high as 27 times / Table 10/.

The fact that the indices of poliomyelitis incidence within the group of internal control in the Bielorussian SSE / contact groups of urban children/ are in excess of the external control / rural areas, not covered by vaccination/ should be explained by a higher frequency of poliomyelitis among the urban children, just as it had been observed during the past years. By evaluating the incidence rate among non=vaccinated children of the internal control in terms of that for the vaccinated ones, we could have anticipated the frequency of the disease among these latter to amount to 33 cases of paralytic poliomyelitis , instead of 2, actually registered.

In the Latvian SSR a total of 242 940 children aged up to 14 were vaccinated during 1959. Among these there was only

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one instance of paralytic poliomyelitis, registered in the period of June-December 1959, as against 15 cases anticipated in accordance with the morbidity data for control groups in districts not covered by immunization with live vaccine.

During all previous years the frequency of poliomyelitis in these districts of external control did not surpass 20% of the morbidity rate recorded in the areas covered by vaccination in 1959. But during the current year - 9 poliomyelitis cases for a total of 141 335 childred aged up to 14 years could be noted in the course of 6 months, this representing 12.8 per 100 000 of population, as against 0.8 per 100 000 among the children of the vaccinated group, or 3.9 per 100 000 among 106 872 children of the internal control.

Thus, the reduction of the incidence rate among those immunized with live vaccine in the Latvian SSR was more than 10 times.

Preliminary data compiled for the Pskov region indicate a 7=fold decrease in the morbidity rate among those immunized with live vaccine.

The study of live vaccine against poliomyelitis, conducted in 1959 under our direction in the Latvian SSR, Bielorussian SSR, Moldavian SSR and in the Russian SFSR on the material embracing 1 800 000 immunized children, has established, both the innocuousness of the preparation made of attenuated A. Sabin's strains and its high epidemiological efficacy.

In all republics and regions where live vaccine was administered to the bulk of the susceptible children within the age bracket of up to 14 years, there occurred radical changes in the seasonal dynamics of the disease, characteristic of poliomyelitis.

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On the territories covered by mass immunization there was no seasonal rise in the poliomyelitis incidence in June-October, which occurred in the same period among children residing in the areas not subjected to immunization with live vaccine.

The number of paralytic poliomyelitis cases among children immunized with live vaccine proved to be quite insignificant , when compared with the non=vaccinated groups of children in the same age=bracket. The efficacy indices for the live vaccine were highest / 15-20 times/ in children of the creche age, who were responsible for the bulk of disease incidence in control groups, and declined in senior groups, with lesser frequency in controls. The mean minimal effectivity index varied in different republics from 6 to 15 times.

The live vaccine proved appreciably more effective than the killed Salk's vaccine, administered three times, when both preparations are studied under maximally comparable conditions.

A fairly high frequency of paralytic poliomyelitis among children of the internal control groups, established in 1959, i.e. in those potentially contacting subjects immunized with live vaccine,is a proof of unreliability and irregularity of " blind" immunization with the circulating vaccinal virus. This lays emphasis upon the necessity of general and compulsary immunization with live vaccine of all underaged, which will ensure the maximal efficacy of the vaccination and will contribute to a far=reaching elimination of "wild" pathogenic viruses.

C O N C L U S I O N S

1. The live vaccine against poliomyelitis prepared from attenuated A.Sabin strains is completely harmless and does not represent any menace of reversion or conversion into increas-

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ingly virulent state of vaccinal strains.

2. The field performance of mass immunization is exceptionally convenient, simple and ensures maximal coverage of the population within very short time=periods, lasting 2-3 weeks per each cycle.

3. The fact that the vaccinated fail to reveal any signs of general or local reactions differing in their frequency from analogous symptoms apparent in the non=vaccinated groups of external control, tends to characterize this preparation to be practically areactogenic. This furnishes sufficient ground to sharply reduce the existing contra=indications to the employment of live vaccine concurrently with other immunization measures.

4. High epidemiological effectivity of live vaccine, ascertained in 1959 as a result of our observations in four republics, which is substantially higher than that of the killed vaccine, fully justifies the suggestion to stop further use of the less effective Salk's vaccine and, beginning from 1960, adopt immunization exclusively with live vaccine.

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It is only the live vaccine that is capable of ensuring factual requirements of the country in an effective immunizing preparation.

5. A fairly high poliomyelitis incidence among non=vaccinated children contacting the immunized ones indicates the need of compulsary use of live vaccine, just as in the case of preparations against smallpox or/and diphtheria. It is only this course of compulsary immunization, conducted under strict state control, that will ensure the solution of a highly important task of gradual elimination of a wild pathogenic strains reservoir, suppress the circulation of these strains and bring about eradication of poliomyelitis as a dangerous mass infection of

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children, which would be quite inevitable under these conditions.

6. To realize mass immunization it is expedient to adopt a course of compulsary triple administration of live vaccine according to the following optimal scheme: first vaccination with the monovaccine of the I type, second inoculation with the divaccine of the II and III types, introduced with an interval of 4-6 weeks. In the light of immunological observations a scheme like this is practical and more advantageous than introduction of monovalent vaccines with the fourth revaccination with the trivaccine, since it secures a twofold administration of the each virus serotype in the course of triple immunization.

7. The age pattern of the population subject to vaccination in 1960 may be limited to the group including 0-20 years, the one in need of immediate immunization. A relatively rare incidence of the disease among senior age groups is called forth by the infection with viruses circulating among the children and adolescents.

8. The eradication of the principal virus reservoir associated with children and adolescents aged below 20 years will undoutedly contribute to the improvement of health condition in the senior age=groups of our population, which can be fitted into the immunization scheme at some later dates of the forthcoming campaign.

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THE QUOTED LITERATURE BY THE SOVIET AUTHORS

1. Bulychev,P.P,Groisman,G.M.,Chalkina,O.M,Dyakova,V.S., Ezhov, N.N., Kovalev,E.E., Steklova,P.M.,Sharapov,B.I.,Shlyakhov,E.N.
The results of the study into the epidemiological efficacy of active immunization with live vaccine against poliomyelitis in the Moldavian SSR.
Live vaccine agaisnt poliomyelitis,L.1960.

2. Vasiliev,KG.,Glinskaya,E.V.
Analysis of reactogenic properties of live vaccine against poliomyelitis according to observations conducted in Riga
Live vaccine against poliomyelitis,L.1960.

3. Vasiliev,K.G.,Glinskaya,E.V.,Kibitkina,E.N., Kukain,R.A., Kurnosova,L.M.,Khvatova,A.Ya.,Khvatov,P.P.
Preliminary results of vaccination against poliomyelitis with attenuated live vaccine in the Latvian SSR.
Live vaccine against poliomyelitis,L.1960.

4. Gorev,N.E.
On the behaviour of the poliomyelitis virus vaccinal strains in the intestinal tract of repeatedly immunized children.
Live vaccine against poliomyelitis,L.,1960.

5. Davidenkova,E.F.,Savelieva=Vasilieva,E.A.
The results of two=year clinical observations of children immunized with attenuated live vaccine against poliomyelitis
J. Neuropathology psychiatry,v.59,790-795,1959

6. Drobyshevskaya,A.I., Klyuchareva,T.E.,Kolesnikova,L.V., Smorodintsev,A.A.
Characteristic features of the live vaccine used in 1959
Live vaccine against poliomyelitis,L.,1960.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

7. Ilienko, V.I., Alekseev,B.P.

Dynamics of the poliomyelits virus propagation in the intestines of children immunized with attenuated live vaccine

Live vaccine against poliomyelitis,L.,1960.

8.Ilienko,V.I.,Kurnosova,L.M.,Zhidova,G.P.,Radionova,R.N.

Materials on the virusological and serological examination of children contacting subjects immunized with attenuated live vaccine against poliomyelitis

Live vaccine against poliomyelitis,L.,1960.

9.Kantorovich,R.A., Zhilova,G.P.,Ostrovsky,G.D.,Rykushina,B.P. Bregantseva,P.V.,Golubeva,L.P.

Experience with mass immunization of children in the Pskov and Novgorod regions with attenuated live vaccine against poliomyelitis

Live vaccine against poliomyelitis,L.,1960.

10.Kardash,I.B.,Votyakov,V.I.,Ilienko,V.I.,Monakhova,O.I.,Selivanov,Ya.m.,Feldman,E.V.,Bondareva,N.V.,Mar,G.I.,Sheremetieva,L.G.

The study of epidemiological efficacy of attenuated live vaccine in the Bielorussina SSR.

Live vaccine against poliomyelitis,L.,1960.

11. Kosmachevsky,V.V., Glazkova,G.S.,Aleksandrova,V.P.

Clinical observations over children of pre=school age immunized enterally with live vaccine against poliomyelitis.

Live vaccine against poliomyelitis,L.,1960.

12. Kurnosova,L.M.,Zhilova,G.P.

Immunological changes in the blood of children immunized with live vaccine against poliomyelitis.

Live vaccine against poliomyelitis,L.,1960.

13. Smorodintsev,A.A.

Theoretical backgrounds for the use of live vaccine

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

against poliomyelitis.

Live vaccine against poliomyelitis,L.,1960.

14. Smorodintsev,A.A.

Methodical directions with respect to the organization and realization of peroral immunization with attenuated live vaccine against poliomyelitis.

Live vaccine against poliomyelitis,L.,1960.

15. Smorodintsev andcollaborators,

Live vaccine against poliomyelitis.

Year=book of t. Institute of the Experimental Medicine for 1957, 301-315,1958.

16. Smorodintsev,A.A. and collaborators.,

Live vaccine against poliomyelitis.

Current problems of immunology,192-309,1959

17. Chumakov,M.P and coll.,

Preliminary communication on the mass peroral immunization of the population against poliomyelitis with live vaccine prepared from attenuated A.Sabin's strains.

18. Chumakov,M.P. and coll.,

Comparative characteristic features of the live vaccine against poliomyelitis.

Problems of virusology,No.5,533-537,1959.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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T.I

THE NUMBERS OF VACCINATED AND OF CONTROL GROUPS IN THE BIELORUSSIAN, LATVIAN, MOLDAVIAN SSR, NOVGOROD AND PSKOV REGIONS IN 1959

Districts	Age-groups	Subjects in the groups under observations		
		Vaccinated	Internal control	External control
Bielorussian SSR	6 mon.-3 yr.	74868	77612	344076
	3 yr.- 7 yr.	119897	152353	614350
	7 yr.-14 yr.	347754	85371	977375
Total		542519	315336	1 935 801
Moldavian SSR	9 mon.-3 yr.	72274	52366	107277
	3 yr.- 7 yr.	80551	42481	109500
	7 yr.-14 yr.	201782	26826	164857
Total		354 607	121 673	381 634
Latvian SSR	9 mon.-3 yr.	27840	56065	32103
	3 yr.- 7 yr.	55349	32752	35744
	7 yr.-14 yr.	159751	18055	73488
	14 yr.-30 yr.	178604		
Total		421544	106872	141 335
Pskov region	9 mon.-3 yr.	49292	7133	-
	3 yr.- 7 yr.	45699	6526	-
	7 yr.-15 yr.	102843	21594	-
Total		197 834	35 253	-
Novgorod region	9 mon.-3 yr.	41438	6979	-
	3 yr.- 7 yr.	39990	3970	-
	7 yr.-15 yr.	80341	13875	-
Total		161 769	24 824	-
Grand total		1 677 273	603 958	2 458 770

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IMMUNOLOGICAL PATTERN OF THE UNDER-AGED POPULATION OF LENINGRAD, NOVGOROD REGION, LATVIAN SSR AND MOLDAVIAN SSR WITH RESPECT TO THE POLIOMYELITIS VIRUS OF VARIOUS TYPES

Age-Groups	I type % of negatives					II type % of negatives					III type % of negative					% of triply negative				
	Leningrad	Novgorod Region	Latvian SSR	Moldavian SSR	Belorussian SSR	Leningrad	Novgorod Region	Latvian SSR	Moldavian SSR	Belorussian SSR	Leningrad	Novgorod Region	Latvian SSR	Moldavian SSR	Belorussian SSR	Leningrad	Novgorod Region	Latvian SSR	Moldavian SSR	Belorussian SSR
0 - 2	77	63	64	64	60	72	87	78	79,2	65	64	82	66	64,4	65	48	48	41	33,6	36
3 - 4	41	31	42	28	45	41	60	50	37,9	54	48	47	35	36,7	50	28	15	20	9,1	22
5 - 6	28	18	25	20	40	38	46	41	25	53	37	35	23	29	26	18	6	6	5	0
7 - 9	29	18	25	20	31	26	42	39	26	37	29	33	29	26	33	14	6	4	4	13
10 - 12	26	11	19	15	35	26	33	34	23	50	37	30	27	22	27	7	4	0	3	20

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SUSCEPTIBILITY TO POLIOMYELITIS OF CHILDREN AND ADOLESCENTS IN THE LATVIAN SSR BEFORE AND 6 MONTHS AFTER TWOFOLD IMMUNIZATION WITH LIVE VACCINE

The age of the examined (years)			Before Vaccination					After vaccination				
			Number of examined	% of subjects with no antibodies to poliomyelitis virus				Number of examined	% of subjects with no antibodies to poliomyelitis virus			
				I type	II type	III type	All the three types		I type	II type	III type	All the three types
0	–	2	55	60	65	55	36	68	19	11,7	19	1,5
3	–	4	22	45	54	50	22	49	8	6,1	8	2
5	–	6	15	40	53	26	0	67	1,5	1,5	4,5	0
7	–	9	45	31	37	33	12	60	1,5	16,6	10	1,6
10	–	12	48	35	50	27	20	51	11,7	11,7	18	0
13	–	15	35	28	31	17	0	31	9,7	3,2	3,2	0
Total			220					326				

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T.

SUSCEPTIBILITY TO POLIOMYELITIS OF CHILDREN IN THE BIELORUSSIAN SSR BEFORE VACCINATION AND 6 MONTHS AFTER TWOFOLD IMMUNIZA TION WITH LIVE VACCINE

The age of examined (years)	Before vaccination					After vaccination				
	Number of examined	% of subjects with no antibodies to poliom. virus				Number of examined	% of subjects with no antibodies to poliomyelitis virus			
		I type	II type	III type	all 3 types		I type	II type	III type	All three types
0-2	67	64	78	66	41	33	0	9	3	0
3-4	45	43	50	35	20	30	10	13	13	0
5-6	44	25	41	23	6	41	10	4,8	22	0
7-9	72	25	39	29	4	67	1,5	1,5	12	0
10-12	43	19	34	27	0	84	3,5	4,7	14	0
13-15	25	16	22	4	0	78	1,2	1	5	0
16-20	22	18	18	10	0	56	9	5,3	16	0
Total	406	1				389				

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T. 3

SEASONAL DYNAMICS OF PARALYTIC POLIOMYELITIS INCIDENCE IN BYELORUSSIA, LATVIA AND MOLDAVIA DURING 1957-1959 IN AREAS COVERED (+) AND NOT COVERED (-) BY VACCINATION IN 1959.

REPUBLICS	Years	Areas covered by immunisation in 1959	Months of the year												Total
			January	February	March	April	May	June	July	August	September	October	November	December	
Byelorussia	1957	-	6 6	6 8	3 5	4 5	4 6	14 21	20 59	30 58	29 43	23 33	6 18	18 24	181 286
	1958	-	11 20	6 10	14 26	6 18	15 13	21 45	62 49	48 53	47 82	35 51	16 51	9 20	228 413
	1959	-	9 8	5 14	5 3	5 14	14 17	9 12	5 19	8 20	6 19	6 11	6 8	1 7	77 135
Latvia	1957	-	11 4	5 -	4 1	2 2	3 -	2 3	6 1	9 4	12 2	13 -	3 -	2 2	72 17
	1958	-	- 2	3 1	1 -	2 -	2 -	3 2	17 3	28 6	18 6	22 1	17 6	10 3	123 30
	1959	-	4 -	2 1	5 -	1 -	- -	1 3	- 6	2 3	- 1	1 2	- -	- -	15 14
Moldavia	1957	-	0 0	0 3	0 0	1 2	0 2	0 1	0 2	0 16	3 25	7 11	8 2	7 2	26 55
	1958	+	1 7	5 17	3 33	3 14	7 3	27 28	30 19	16 22	28 17	12 4	5 0	3 2	140 151
	1959	-	4 5	5 1	2 7	3 1	1 1	4 5	1 4	2 11	0 10	1 13	1 3	1 1	25 62

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T.5

THE NUMBER OF PARALYTIC CASES OCCURRING DURING THE EPIDEMIC SEASON OF 1959 IN THE AREAS OF BIELORUSSIA, LATVIA AND MOLDAVIA COVERED AND NOT COVERED BY IMMUNIZATION

Republic	Age-groups	Non-vaccinated (external control)			non-vaccinated (external control)			Population Census	Immunized with live vaccine		The number of anticipated poliomyelitis cases
		Census of population	No. of cases Total	Convent. index per 100 000 of inhabitants	Population census	No. of cases Total	Conventional index per 100 000 of popul.		No. of cases Total	Conventional index per 100 000 of popul.	
Bielorussia	6 m.- 3 yr.	344076	82	5,7	77612	35	67,3	74868	2	4,0	33
	4 yr.-7 yr.	614350	23	5,6	15.353	10	9,9	119897	3	3,7	7
	8 yr.-14 yr.	977375	12	1,8	85371	2	3,5	347754	1	0,4	8
	Total	1935801	117	9,4	315336	47	22,0	542519	6	1,6	48
Moldavia	9 m.- 3 yr.	79066	36	78,2	37744	7	31,8	72274	2	4,1	36
	4 yr.-7 yr.	66886	4	10,5	23870	0	0	80551	0	0	3
	8 yr.-14 yr.	164857	1	1,0	24280	0	0	201782	0	0	0
	0-7 yr.(immunized with Salk vaccine)	70825	6	14,7	32820	1	5,1				
	Total	381634	47	21,9	121673	8	8,5	354607	2	0,8	39
Latvia	9 m. -3 yr.	32103	1	6,2	36065	2	7,1	27840	0	0	1
	3 yr.-7 yr.	35744	3	16,8	32752	0	0	55349	0	0	4
	7 yr.-14 yr.	73488	5	13,6	18055	0	0	159751	1	1,2	10
	Total	141335	9	12,8	106872	2	3,9	242940	1	0,8	15

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ANALYSIS OF POLIOMYELITIS INCIDENCE IN BYELORUSSIA DURING 8 MONTHS OF 1959

T.7

	Age-groups	Number of children in age-groups		Number of poliomyelitis cases by months								Total for 8 months	Mean annual index per 100,000 children	Expected number of cases
			per cent	May	June	July	August	September	October	November	December			
Immunized with live vaccine	6 mo.-3 yr.	74868	13,8	1	–	–	1	–	–	–	–	2	4,0	33
	4 yr.-7 yr.	119807	22,1	–	–	–	–	1	2	–	–	3	3,7	7
	8 yr.-14 yr.	347754	64,1	–	–	–	–	1	–	–	–	1	0,4	8
	Total	542519	100	1	–	–	1	2	2	–	–	6	1,3	48
Non-vaccinated (internal control)	6 mo.-3 yr.	77612	24,6	10	4	3	6	4	4	3	1	35	37,3	
	4 yr.- 7 yr.	152358	48,3	1	5	2	1	–	–	1	–	10	9,9	
	8 yr.-14 yr.	85871	27,1	–	–	–	–	–	–	2	–	2	3,5	
	Total	315836	100	11	9	5	7	4	4	6	1	47	22,0	
Non-vaccinated (external control)	6 mo.-3 yr.	344076	17,7	13	8	17	14	4	7	4	5	82	35,7	
	4 yr.-7 yr.	614360	31,7	3	3	3	4	4	2	2	2	23	9,5	
	8 yr.-14 yr	977375	50,4	1	1	–	2	1	2	5	–	12	1,8	
	Total	1935801	100	17	12	20	20	19	11	11	7	117	9,0	

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DISTRIBUTION OF PARALYTIC POLIOMYELITIC CASES IN JUNE–DECEMBER 1959 ACCORDING TO THE TERRITORIES
COVERED AND NOT COVERED BY IMMUNIZATION WITH LIVE VACCINE IN THE MOLDAVIAN SSR

T.8

Groups	Kind of vaccination	Age	Numerical composition of groups	%	The number of paralitic VI	VII	VIII	IX	X	XI	XII	Total	Conventional index in estimating per 100 000 p.	Number of anticipated cases
I	Immunized with live vaccine	9 m.–3 yr.	72274	20,4	–	–	2	–	–	–	–	2	4,1	36
		3yr.–7 yr.	80551	22,7	–	–	–	–	–	–	–	–	–	3
		7yr.–14yr	201782	56,9	–	–	–	–	–	–	–	–	–	–
Total			354607	100,0	–	–	2	–	–	–	–	2	0,8	39
II	Immunized with Salk vaccine (triple)	9 m.–3 yr.	14622	12,0	I	–	–	–	–	–	–	I	11,6	
		3yr.–7 yr.	15611	12,8	–	–	–	–	–	–	–	–	–	
		7yr.–14yr.	2587	2,0	–	–	–	–	–	–	–	–	–	
		Total	32820	26,8	I	–	–	–	–	–	–	I	5,1	
III	non-vaccinated (internal control)	9 m.– 3yr.	37744	31,1	3	I	–	–	I	I	I	7	31,8	
		3yr.– 7yr	26870	22,2	–	–	–	–	–	–	–	–	–	
		7 yr.–14yr	24239	19,9	–	–	–	–	–	–	–	–	–	
		Total	88853	73,2	3	I	–	–	I	I	I	7	13,5	
	Total		121673	100,0	4	I	–	–	I	I	I	8	10,7	
IV	Non-vaccinated external control)	9 m.– 3yr.	79066	20,7	4	2	9	9	10	I	I	36	78,2	
		3yr.–7yr.	66886	17,8	I	–	I	I	I	–	–	4	10,5	
		7yr. –14yr	164857	43,4	–	–	–	–	–	I	–	I	1,0	
		Total	310809	81,4	5	2	10	10	11	2	I	41	22,5	
V	Immunized with Salk vaccine	9 m.– 3yr.	28211	7,4	–	–	I	–	2	–	–	3	18,0	
		3yr.– 7yr.	42614	11,2	–	I	I	–	–	I	–	3	11,8	
		7yr.–14yr.	0	0	–	–	–	–	–	–	–	–	–	
		Total	70825	18,6	–	I	2	–	2	I	–	6	14,7	
Global			381634	100,0	5	3	12	10	13	3	I	47	21,9	

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STAT

MATERIALS ON IMMUNOLOGICAL AND EPIDEMIOLOGICAL EFFICACY OF LIVE VACCINE AGAINST POLIOMYELITIS

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The large=scale use in recent years of Salk killed vaccine to control poliomyelitis has not eliminated the threat of acute anterior poliomyelitis developing in triply incoculated children and has failed to influence the virus circulation in childrens' establishments. Restricted duration of the post=vaccinal immunity required repeated immunization following a completed cycle of triple inoculations with the killed vaccine.

The necessity to sacrifice vast numbers of monkeys to prepare each and every million doses of killed vaccine has already become a source of considerable difficulties in securing the needed stock of monkeys for the ever=increasing production of this preparation.

At present the large=scale output of a complex, costly and insufficiently effective Salk vaccine, which necessitates inflicting additional traumas to children by repeated injections, can be entirely dispensed with in view of the possible complete replacement of the killed vaccine with a more effective, fully harmless, maximally convenient and accessible live one, administered perorally and prepared from the A.Sabin or G.Koprovsky strains /13/.

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The live vaccine is devoid of principal defects specific to that of Salk. It is not only capable of producing a lasting humoral immunity, which precludes viral invasion into the central nervous system, but tends also to make the intestinal tract highly insusceptible, this ruling out the development of the causative agent in a receptive organism. The live vaccine is the groundstone for future solution of a major epidemiological task- that of limiting and eradicating a vast ocean of highly pathogenous "wild" viruses, tightly surrounding our adolescent population- an undertaking entirely outside the scope of the killed vaccine.

It was thanks to the investigations of our laboratory, effected in 1956-1958, that the broad study into the epidemiological effectivity of live vaccine against poliomyelitis, obtained from the A.Sabin's strains, could be organized. This was effected in the USSR during 1959 by the Institutes of Experimental Medicine and Poliomyelitis of the AMS of the USSR and covered 3 million children, vaccinated in the period of April-May, prior to the seasonal upsurge of the disease. In those years we had assumed great resposibility in testing the innocuousness and immunogenic properties of the Sabin's vaccinal strains on progressively increasing numbers of children belonging to junior age groups, which, by the end of 1958, permitted us to give positive answear as to the innocuous nature and efficacy of live vaccine, this having been the basic point of our reaearch. The positive solution of the problem rested on the data of the laboratory and clinical examination covering 2500 healthy children of the creche and pre=school age groups, immunized with live vaccine preparaed in Leningrad /15/.

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The results of this work, carried out in close contact with the clinic for nervous diseases of the Leningrad medical pediatric institute (E.F.Davidenko) and Infectious clinic of the Leningrad Sanitary=Hygienic Medical Institute (V.V. Kosmachevsky) proved complete harmlessness of the live vaccine, both to the vaccinated children and to susceptible groups of non=vaccinated adolescents immediately contacting the latter.

Observations carried out for a space of two years and covering both the inoculated and non=inoculated children bore out that the live vaccine did not produce any leasions of the central nervous system, reproducible of even the mildest forms of meningeal poliomyelitis, failed to affect the intestinal tract, respirative tract or any other organs. In those inoculated with live vaccine even the temperature reaction was of a very rare occasion and its frequency was similar to that encountered in analogous establishments for children, where live vaccine was not introduced at all. (2,5,11).

Observations have established high immunogenous activity of live attenuated vaccine for susceptible children, provided its repeated administration was in the form of monovalent vaccines. A somewhat lower activity was achieved by a single pediatric institute [illegible] combined divaccine or trivaccine.

A consecutive triple immunization of susceptible children with monovalent preparations of live vaccine against poliomyelitis of the I,II and III types ensures obtaining of comparable indices for a quantitative rise in the number of antibodies, irrespective of the order in which alternate individual serotypes of the vaccine. It has been noted that the indices showing the antibody rise against the virus of the III type are regularly behind those of humoral immunity with

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respect to the I and II types (12).

The groups of susceptible children who responded by development of humoral immunity to a single introduction of monovalent vaccines comprise 90-95% for the vaccines of the I and II types and around 80-90% for those of the III type. Revaccination of triply inoculated children with the polyvalent vaccine of the I,II and III types corrects the shortcomings of the first round of immunization and imparts complete immunity to the greatest part of refractory children.

The prepared polyvalent vaccine containing 100 000 of tissue cytopathogenic units of each virus type represents a most appropriate form of universal preparation adaptable for practical use.

Single administration of trivaccine stimulates a somewhat lower level of antibodies to all three types, as compared with the triple introduction of a monovalent vaccine or divaccine, but twofold and, particularly, triple administration of trivaccine ensures immunological changes approaching a 100% level.

Exceptionally convenient, speedy and effective is triple immunization effected along the following scheme: monovaccine of the I type, divaccine of the II and III types, all of these conducted with an interval of 1 month. This scheme secures maximal immunological efficacy and requires the same amount of the preparation as the triple introduction of monovaccines, with subsequent revaccination in 1-3 months. Its merit lies in the rapid completion of the entire immunization cycle, without encumbering the medical staff with the performance of the fourth revaccination.

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The high immunogenous effect of live vaccine is associated with the propagation of vaccianl viruses in the intestinal canal of inoculated children, which follows a rigid cyclic pattern with the maximum accumulation of the virus between the 7-21 days and subsequent gradual decline in its concentration during the further 15-20 days.

The multiplication of the virus is of a highly regular character, provided there is not interference with other viruses, and it reaches its maximal intensity in children with a low level of immunity to poliomyelitis, while in subjects whose blood comprises specific antibodies- it tends to show a progressive decline.

The major feature peculiar to the live vaccine was the fact that it helped to form intensive and prolonged resistance of the intestinal tract to repeated introduction of maximal doses of homologous viruses, whereby these fail to propagate and are swiftly eliminated from the intestinal canal/4/.

On rare occasions the repeatedly administered virus displays its ability to multiply, but the intensity of this process is by far inferior to the initial propagation intensity of the virus in the same child.

Long=term observations of the intestinal canal immunity in children inoculated for a period of 4-24 months by live vaccine have demonstrated that their revaccination at the above dates, following the first inoculation, tends to confirm the maintainance of an intensive and regular immunity of the intestinal canal to the repeated infection with the vaccinal strain.

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The resistance of the intestinal tract in children to the primary introduction of vaccinal strains stands in direct relationship with the state of their humoral immunity to the homologous virus. With low initital titres of virus=neutralizing antibodies / 1:4-1:16/ the intestinal tract was noted to possess poor resistance to its invasion with vaccinal strains. On the other hand, with elevated titres of antibodies there is either no propagation of vaccinal strains at all, or they develop slowly within a very short space of time.

To secure lasting and intensive resistance / local/ of the intestinal tract, of importance is garanteed inoculation with a high=quality vaccine, in view of unreliable results of immunization developing after contacts with non=vaccinated children.

In the main, the results of vaccination are dependent upon the dose of the preparation actually introduced, and also on the state of specific and non=specific immunity of the children subject to inoculation.

Liquid vaccine comprising $10^{7.0}$ - $10^{7.5}$ TCU_{50} of the vaccine represents a garanteed preparation for peroral immunization against poliomyelitis, which ensures maximal uniformity and standard dosage for individual children.

Intensive discharge of vaccinal strains from the intestine of vaccinated children, occurring during the first month after immunization, produces natural dissemination of the vaccinal virus among susceptible subjects, coming in contact with the vaccinated ones/8/.

This process of the vaccinal virus extending and covering the contact groups is one of the most characteristic features of the live vaccine against poliomyelitis, creating conditions

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favorable for involving into the immunization process of those who come in contact with the immunized groups of the population, and also producing possibilities for revaccination of those already inoculated.

There should be, however, no overestimation of the factual epidemiological significance of such a " blind" immunization. Thus, for example, the enclosed herewith materials, obtained in 1959 as a result of epidemiological observations covering Bielorussian and Moldav republics were indicative of the fact, that non-vaccinated groups of children who were in potential contact with the vaccinated ones showed a fairly high incidence of acute anterior poliomyelitis, differing very little from the morbidity rate registered for the population sections with no actual contacts with the vaccinated.

"Blind" infection with vaccinal virus reaches its maximal intensity among children in the junior age bracket, for instance, in creches. With the increasing age of children the indices for contact infection show a rapid decline of intensity (children of pre-school and, particularly, school age/, so that in susceptible adults the indices for the contact spread of vaccinal virus are minimal.

Great attention was paid by us to the cardinal question of possible reversion of Sabin's vaccinal strains to their initial pathogenic variant, following frequent and prolonged passages via the intestinal tract of susceptible children/15,16/.

The study of changes in the neurotropic activity of vaccinal strains in monkeys, following prolonged artificial or natural passages through susceptible children, revealed the appearance of periodic and relatively slight intensification of

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neurotropic properties in vaccinal strains, which,however, did not lead to a progressive rise in their neurovirulence.

These data of ours were , in a large measure, responsible for putting an end to a very pointed discussion on the dangers connected with the reversion of the vaccinal strains group investigated by us.

The data confirming the innocuous nature of the vaccine made it possible for the Commission on Sera and vaccines and the Board of the Ministry of Public Health of the USSR to permit in November 1958 to undertake large=scale epidemiologic observations with the view of investigating the harmlessness of the live poliomyelitic vaccine.

In April and May 1959 we utilized the stocks of live vaccine at the disposal of the Virusology Department of AMS Institute of Experimental Medicine, amounting to about 2.000 0000 doses for immunization of 1.700 000 adolescents aged up to 14-18 years in Bielorussian, Latvian and Moldavian republics,while in June=July 1959 we carried out similar vaccinations in Pskov and Novgorod regions with the vaccine obtained from the AMS USSR Institute for the Study of Poliomyelitis. The vaccination was effected twice: the first / in April 1959/ with the monovaccine of the I type, and the second /in May 1959/- with divaccine of the II and III types.

BASIC PRINCIPLES UNDERLYING THE ORGANIZATION OF VACCINATIONS AND THE STUDY OF EPIDEMIOLOGICAL EFFECTIVITY OF THE LIVE VACCINE

The Ministries of the Union Republics responsible for the vaccinations made arrangements in advance to instruct in detail the chief physicians and epidemiologists of the district

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sanitary=epidemiological stations about the tasks and procedures of vaccination and, together with them, compiled a detailed schedule of vaccinations and drew up personal lists of vaccination teams at a rate of 300-500 vaccinations per day for 1 team, including one physician / feldsher/ and 2 qualified nurses.

Analogous work was performed in every city or district, with all members of the medical staff participating in the immunization summoned up to receive appropriate instructions.

Official institutions responsible for the vaccination sent their permanent representatives to each city or district, who were to stay there for the whole period of immunization and assist in its proper execution.

Prior to vaccination and during its performance there was organized large=scale health=educational work with the view of familiarizing parents and administration of childrens' establishments with the tasks and importance of vaccination.

In organized bodies of children vaccination was done right on the spot. Children not attending such establishments were vaccinated at childrens' polyclinics covering respective residential areas, or during house to house visits.

All vaccinated children and also non=vaccinated ones, who for different reasons were dispensed from immunization, were registered by the vaccination teams with their names entered either into special lists or put on individual unified forms, compiled separately for each childrens' establishment or residential area. The lists were to contain basic information on the vaccinated and the data on preceding vaccinations against poliomyelitis.

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The district epidemiologist summed up in a standard report on vaccinations all records relative to their actual performance, according to individual establishments or villages. A copy of this report was sent to the regional sanitary-epidemiological station or to the local institute of epidemiology and microbiology, which generalized the results of each vaccination.

To study the poliomyelitis incidence in 1959 and epidemiological efficacy of vaccination against poliomyelitis a scientific group was set up in each republic, including clinicians and epidemiologists, appointed by a special order of the Ministry. The task of these groups was an expert investigation of each notified poliomyelitis case within the areas covered by vaccination and deciding on diagnosis in questionable or controversial instances.

In order to study the epidemiological efficacy of active immunization against poliomyelitis two control groups were placed under observation on the territory of each republic or region. The first of them included non-vaccinated children standing in direct or potential contact with the vaccinated ones on the territory covered by immunization with live vaccine/ internal control/. The second control group comprised children and adolescents at the age of up to 14-18 years, residing in areas not covered by the immunization with live vaccine /external control/.

In selecting groups to be immunized with live vaccine it was recommended to cover territories with maximal poliomyelitis incidence in the past years, leaving areas with a lower morbidity rate to serve as external controls.

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The vaccination coverage did not exceed 50-75% of the population figure for districts subject to immunization.

To arrive at a well-grounded evaluation of the epidemiological efficiency of the live vaccine we endevoured to safeguard the following conditions:

1. Securing comprehensive information on the incidence of the disease in all three groups of vaccinated and non-vaccinated population. The following special measures were undertaken to assure complete detection of all cases of acute anterior and non-paralytic variants of poliomyelitis:

1. Right from the start of vaccinations a system of urgent notifications was introduced by an order of the Ministry of the union republic, covering each case diagnosed as poliomyelitis in any part of the republic or region.

These notifications, including brief information on the diseased, were transmitted either by telephone or wired to the local republican sanitary-epidemiological station or to the institute of epidemiology and microbiology.

2. From among the organized groups of travelling neuropathologists a specialist would be urgently sent to the pertinent area, to verify the diagnosis and collect basic materials for virusological and laboratory investigations (feces of the diseased and first venous blood test. The second blood test was made 3-4 weeks following the onset of the disease.)

3. The poliomyelitis patients were hospitalized in central in-patient departments of regional and republican hospitals, immediately upon the onset of the disease, and when this was impossible,- after termination of the acute period of the disease. Experienced neuropathologists made accurate diagnosis in each individual case, or verified the correctness of the primary clininical diagnosis, with due consideration of laboratory

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investigations.

4. In order to analyse the epidemiological effectivity the figures for recorded cases were used separately according to groups of acute anterior and non-paralytic variants of poliomyelitis. Beside the acute anterior form the group of paralytic poliomyelitis also included the more authentic variants of spinal and bulbo-spinal affections with residual manifestations. The pontine variants, among which predominant were affections of non-poliomyelitic nature, were included in the group of non-paralytic poliomyelitis.

5. The analysis of the epidemiological effectivity rested upon the data of the incidence rate, recorded during the whole period of the epidemiological rise in the intensity of the disease, covering no less than [illegible] months of observations. The processing of the materials relative to the efficacy of vaccinations was timed so as to encompass the period of June-December [illegible], which commenced [illegible] weeks after completion of the second immunization.

II. As a quality index for recording of epidemiological effectivity of vaccination served the scope of laboratory investigations covering registered cases of the disease, including comprehensive feces examination in majority of patients figuring under the diagnosis of poliomyelitis. It was recommended that the materials should be obtained not later than on the [illegible]th day upon the onset of the disease, repeated collection of feces be made in the first days of the affection, with their investigation performed separately, or after [illegible] combination of all specimens.

In addition to virusological examinations of feces, which

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demonstrated excretion of poliomyelitis virus of the I type in 50% of the examined and those of the II and III types - in 15%, we also conducted serological investigations of the patients.

In instances of dubious clinical diagnosis positive laboratory data permitted it to include such patients in the poliomyelitis group. Investigated cases with negative laboratory data, but positive clinical diagnosis were also considered as poliomyelitis.

III. A very important pre=requisite for the performance of epidemiological analysis relative to the efficacy of vaccinations was the availability of accurate information on the numerical age=composition within the categories of children and adolescents covered by immunization with live vaccine and included in the groups of internal and external controls/Table I/.

The local statistical agencies furnished information on the age=distribution of the population inside the territories covered and not covered by vaccinations for all of the above=cited groups.

During vaccinations measures were taken to secure accurate registration of immunised children by using either individual forms or registration lists, with the primary analysis of the age=distribution among the vaccinated at the district sanitary=epidemiological stations.

The above information, compiled in a standard form, was summed up by the sanitary=epidemiological stations or by the epidemiological department of the Institute of epidemiology and microbiology.

If in the given republic or region there happened to be a fairly large group of children covered by triple immunization

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with the killed Salk vaccine we abstained from immunizing them with the live vaccine, but put them on record as a separate group, which would provide us the solution of the question as to the comparative efficacy of the live and killed vaccine under comparable epidemiological conditions.

DISTRIBUTION OF VACCINATED AND CONTROL GROUPS IN DIFFERENT REPUBLICS

In the Bielorussian republic a total of 542 519 children were encompassed by the immunization. They were urban inhabitants with the age of up to 14 years. Numerically this meant 63% of the entire urban population of under-aged. The remaining 37% of children / 315 336/ constituted a group of internal control. The children of rural districts, whose number exceeded that of the urban ones in the same age bracket by 2.5 times, were not subject to immunization with live vaccine and they constituted the group of external control. In the past years the absolute number of poliomyelitis cases among children of the rural and urban groups was approximately equal, this being due to a relatively lower poliomyelitis incidence rate in rural areas during the past years. /10/.

In the Moldavian SSR vaccinations covered 13 central districts of the republic and 4 large cities situated in the midst of them, whose inhabitants make up somewhat over one half of the entire population of the republic. In previous years this territory accounted for about 50% of poliomyelitis morbidity. The total number of vaccinated children and adolescents comprised 407 530 in the age group ranging from 9 months to 18 years. 156 531 subjects were in the group of internal control and 482 430, within the same age bracket, constituted external controls (1).

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In the Latvian SSR the vaccinated children and adults numbered 400 000. They came from Riga and from a number of other districts of the republic and their maximal age was 30 years (3).

Somewhat later, in June and July, the object of immunization were the cities and villages of Novgorod and Pskov regions, were it embraced about 400 000 children with the age of up to 14 years, the proportion of non=vaccinated children in the same age bracket amounting to 20%. (4).

In all republics vaccinations were performed twice, with an interval of 1 month; the first immunization with the vaccine of the I type was made in April, the second, with divaccine of the II and III types - in May 1959. The study of the epidemiological effectivity of vaccinations was started from June 1 1959 i.e.- 2 weeks after termination of the second immunization and 1 1/2 months following completion of the first immunization.

THE STUDY OF THE IMMUNOLOGICAL PATTERN OF THE POPULATION BEFORE AND AFTER VACCINATION.

It is well known how important are humoral indices of the blood in children and adults for the epidemiological prognosis of poliomyelitis and for well=substantiated assessment of the immunization results.

When commencing immunization with live vaccine we made preliminary determinations of the proportion of subjects susceptible to poliomyelitis within different age groups of the population undergoing vaccination with respect to various serotypes of the vaccine. . To do this, the sera of population groups under examination, taken prior to vaccination, were made subject to color test in a dilution of 1:4, together with 100 cytopathogenic doses of the virus and renal cells of

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[illegible] [illegible] and [illegible].

By [illegible] material [illegible] from over [illegible] examined sera it could be established that in different geographical zones of the USSR there exists a fairly large stratum of susceptible children, whose proportion attains the maximal figure for the age-bracket of 2-4 years (60% and above), and then gradually goes down as the age increases up to 16-20 years (Table 2).

Parallel investigation[3] of all negative sera in the reaction of cytopathogenic activity neutralization in monostratal tissue cultures indicated the need for diminishing the color test index by 15-30%. In consideration of the fact that a similar correction is required also for the sera of those examined with color test after vaccination, we - we decided to adopt the percentage of negative sera as a conventional index of factual susceptibility.

The evaluation of [illegible] susceptible subjects made on the basis of calculated indices showing the percentage of negative sera testify to the fact that over 15% of the population comprising the districts under examination were susceptible to one of the poliomyelitis virus serotypes, while [illegible] were among those maximally susceptible (triply negative). Table 3 presents an example of such evaluation for the vaccinated inhabitants of the Moldavian SSR.

With the proportion of susceptible children amounting to 15% out of the total of [illegible] 000 vaccinated we had no less than 400 000 subjects susceptible to the virus of the I, II and III types and over [illegible] 000 triply negative children. It is to be noted that, in spite of the fact that hundreds thousands of

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children were given sumultaneously a highly active vaccinal - virus, which thereby joined in the intensive circulation among the contact children, we not only failed to observe any rise- in the poliomyelitis incidence during the first months following immunization on the territories covered by vaccinations, but , quite the contrary,could mark a distinct decline of the polio- myelitis morbidity, when compared with the anticipated indices, figured out on the basis of the disease incidence among external controls, where no live vaccine had been introduced.

The twofold immunization carried out in April and May 1959 has brought substantial changes into the immunological pattern of the population by curtailing the percentage of sus- ceptible children and adolescents to 1/4-1/8 of the original figure /Tables 4,5,6/.

The third immunization, completed in a number of places and effected with the trivaccine containing 100 000 cytopatho- genic doses of each type, called forth additional and very sub- stantial changes in the numerical level of antibodies, thereby reducing the proportion of susceptible population within the groups of children exposed most to the hazards of the infection / age=bracket 0-4 years/ down to 2-5%.

The above results testify to a high immunological efficacy of the live vaccine employed in triple immunization with the monovaccine of the I type, divaccine of the II and III types and trivaccine of the I+II and III types, which tends to almost entirely eliminate the susceptibility among the population, and protects it against all of the three virus serotypes.

THE EFFECT OF VACCINATION ON THE SEASONAL DYNAMICS OF POLIOMYELITIS AND ITS INCIDENCE RATE

Of high significance is the dynamics of paralytic polio- myelitis cases in the Bielorussian,Latvian and Moldavian repub-

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lics , as well as in the Novgorod and Pskov regions of the Russian Federation. There,among the massively vaccinated population, for the first time in recent years noteworthy was almost complete absence of the seasonal incidence rise in June-October, which had been a regular feature for these areas. This observation could be also confirmed in the instance of contact groups of non=vaccinated children (internal control) , whose numbers sharply decreased on the territories covered by immunization in connection with the vaccination of a large proportion of under=aged population. Radical changes in the usual for these areas seasonal dynamics of poliomyelitis serves as a convincing illustration for the effectivity of the live vaccine. (Table 7).

This can be demonstrated in a most clear=cut fashion by the data showing the distribution of paralytic poliomyelitis cases, registered during the period subsequent to vaccination, i.e. June=December 1959, among children of different age=groups vaccinated and non=vaccinated with live vaccine in different republics (Table 8).

Particularly demonstrable results in favour of the efficacy of live vaccine were obtained during May-December in the Bielorussian SSR. Among the total of 74 868 children aged up to 3 years and inoculated with live vaccine during the months of May-December 1959 on records were only two cases of paralytic poliomyelitis. At the same time, among 77 612 non=vaccinated children of the same age, who were in potential contact with the immunized ones, the number of paralytic cases amounted to 35. This means a reduction in the incidence of the disease among vaccinated 17.5 times over and above the anticipated figure, and with respect to the morbidity rate among external controls- 8.5 times over that level.

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The efficacy of live vaccine in senior groups of pre=school and school ages is represented by an index equal to 2-3, this being due to a low poliomyelitis incidence rate in respective control groups (4.0 per 100 000 for children of 7-14 age bracket) The summary morbidity index for the whole group of vaccinated comprised 1.6 per 100 000,22.0 per 100 000 for internal control and 9.0 per 100 000 for external control / Table 9/.

In the Moldavaian SSR 2 cases of paralytic poliomyelitis were registered for a total of 354 607 vaccinated children aged up to 14 years. In the group of internal control which numbered 88 853 subjects, i.e. 1/3 of the vaccinated group on records were 7 instances of paralytic poliomyelitis, this signifying a fall in the incidence of the disease by over 8 times. As contrasted with non=vaccinated groups of external control, where altogether 41 cases of the disease came upin a total of 310 809 children, or 22.5 per 100 000, the decline in the morbidity rate is as high as 27 times / Table 10/.

The fact that the indices of poliomyelitis incidence within the group of internal control in the Bielorussian SSE / contact groups of urban children/ are in excess of the external control / rural areas, not covered by vaccination/ should be explained by a higher frequency of poliomyelitis among the urban children, just as it had been observed during the past years. By evaluating the incidence rate among non=vaccinated children of the internal control in terms of that for the vaccinated ones, we could have anticipated the frequency of the disease among these latter to amount to 33 cases of paralytic poliomyelitis , instead of 2, actually registered.

In the Latvian SSR a total of 242 940 children aged up to 14 were vaccinated during 1959. Among these there was only

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one instance of paralytic poliomyelitis, registered in the period of June-December 1959, as against 15 cases anticipated in accordance with the morbidity data for control groups in districts not covered by immunization with live vaccine.

During all previous years the frequency of poliomyelitis in these districts of external control did not surpass 20% of the morbidity rate recorded in the areas covered by vaccination in 1959. But during the current year - 9 poliomyelitis cases for a total of 141 335 childred aged up to 14 years could be noted in the course of 6 months, this representing 12.8 per 100 000 of population, as against 0.8 per 100 000 among the children of the vaccinated group, or 3.9 per 100 000 among 106 872 children of the internal control.

Thus, the reduction of the incidence rate among those immunized with live vaccine in the Latvian SSR was more than 10 times.

Preliminary data compiled for the Pskov region indicate a 7-fold decrease in the morbidity rate among those immunized with live vaccine.

The study of live vaccine against poliomyelitis, conducted in 1959 under our direction in the Latvian SSR, Bielorussian SSR, Moldavian SSR and in the Russian SFSR on the material embracing 1 800 000 immunized children, has established, both the innocuousness of the preparation made of attenuated A. Sabin's strains and its high epidemiological efficacy.

In all republics and regions where live vaccine was administered to the bulk of the susceptible children within the age bracket of up to 14 years, there occurred radical changes in the seasonal dynamics of the disease, characteristic of poliomyelitis.

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On the territories covered by mass immunization there was no seasonal rise in the poliomyelitis incidence in June-October, which occurred in the same period among children residing in the areas not subjected to immunization with live vaccine.

The number of paralytic poliomyelitis cases among children immunized with live vaccine proved to be quite insignificant , when compared with the non=vaccinated groups of children in the same age=bracket. The efficacy indices for the live vaccine were highest / 15-20 times/ in children of the creche age, who were responsible for the bulk of disease incidence in control groups, and declined in senior groups, whith lesser frequency in controls. The mean minimal effectivity index varied in different republics from 6 to 15 times.

The live vaccine proved appreciably more effective than the killed Salk's vaccine, administered three times, when both preparations are studied under maximally comparable conditions.

A fairly high frequency of paralytic poliomyelitis among children of the internal control groups, established in 1959, i.e. in those potentially contacting subjects immunized with live vaccine,is a proof of unreliability and irregularity of " blind" immunization with the circulating vaccinal virus. This lays emphasis upon the necessity of general and compulsary immunization with live vaccine of all underaged, which will ensure the maximal efficacy of the vaccination and will contribute to the a far=reaching elimination of "wild" pathogenic viruses.

C O N C L U S I O N S

1. The live vaccine against poliomyelitis prepared from attenuated A.Sabin strains is completely harmless and does not represent any menace of reversion or conversion into increas-

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ingly virulent state of vaccinal strains.

2. The field performance of mass immunization is exceptionally convenient, simple and ensures maximal coverage of the population within very short time=periods, lasting 2-3 weeks per each cycle.

3. The fact that the vaccinated fail to reveal any signs of general or local reactions differing in their frequency from analogous symptoms apparent in the non=vaccinated groups of external control, tends to characterize this preparation to be practically areactogenic. This furnishes sufficient ground to sharply reduce the existing contra=indications to the employment of live vaccine concurrently with other immunization measures.

4. High epidemiological effectivity of live vaccine, ascertained in 1959 as a result of our observations in four republics, which is substantially higher than that of the killed vaccine, fully justifies the suggestion to stop further use of the less effective Salk's vaccine and, beginning from 1960, adopt immunization exclusively with live vaccine.

It is only the live vaccine that is capable of ensuring factual requirements of the country in an effective immunizing preparation.

5. A fairly high poliomyelitis incidence among non=vaccinated children contacting the immunized ones indicates the need of compulsary use of live vaccine, just as in the case of preparations against smallpox or/and diphtheria. It is only this course of compulsary immunization, conducted under strict state control, that will ensure the solution of a highly important task of gradual elimination of a wild pathogenic strains reservoir, suppress the circulation of these strains and bring about eradication of poliomyelitis as a dangerous mass infection of

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children, which would be quite inevitable under these conditions.

6. To realize mass immunization it is expedient to adopt a course of compulsary triple administration of live vaccine according to the following optimal scheme: first vaccination with the monovaccine of the I type, second inoculation with the divaccine of the II and III types, introduced with an interval of 4-6 weeks. In the light of immunological observations a scheme like this is practical and more advantegeous than introduction of monovalent vaccines with the fourth revaccination with the trivaccine, since it secures a twofold administration of the each virus serotype in the course of triple immunization.

7. The age pattern of the population subject to vaccination in 1960 may be limited to the group including 0-20 years, the one in need of immediate immunization. A relatively rare incidence of the disease among senior age groups is called forth by the infection with viruses circulating among the children and adolescents.

8. The eradication of the principal virus reservoir associated with children and adolescents aged below 20 years will undoutedly contribute to the improvement of health condition in the senior age=groups of our population, which can be fitted into the immunization scheme at some later dates of the forthcoming campaign.

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THE QUOTED LITERATURE BY THE SOVIET AUTHORS

1. Bulychev,P.P,Groisman,G.M.,Chalkina,O.M,Dyakova,V.S., Ezhov, N.N., Kovalev,E.E., Steklova,P.M.,Sharapov,B.I.,Shlyakhov,E.N.
The results of the study into the epidemiological efficacy of active immunization with live vaccine against poliomyelitis in the Moldavian SSR.
Live vaccine agaisnt poliomyelitis,L.1960.

2. Vasiliev,KG.,Glinskaya,E.V.
Analysis of reactogenic properties of live vaccine against poliomyelitis according to observations conducted in Riga
Live vaccine against poliomyelitis,L.1960.

3. Vasiliev,K.G.,Glinskaya,E.V.,Kibitkina,E.N., Kukain,R.A., Kurnosova,L.M.,Khvatova,A.Ya.,Khvatov,P.P.
Preliminary results of vaccination against poliomyelitis with attenuated live vaccine in the Latvian SSR.
Live vaccine against poliomyelitis,L.1960.

4. Gorev,N.E.
On the behaviour of the poliomyelitis virus vaccinal strains in the intestinal tract of repeatedly immunized children.
Live vaccine against poliomyelitis,L.,1960.

5. Davidenkova,E.F.,Savelieva=Vasilieva,E.A.
The results of two=year clinical observations of children immunized with attenuated live vaccine against poliomyelitis
J. Neuropathology psychiatry,v.59,790-795,1959

6. Drobyshevskaya,A.I., Klyuchareva,T.E.,Kolesnikova,L.V., Smorodintsev,A.A.
Characteristic features of the live vaccine used in 1959
Live vaccine against poliomyelitis,L.,1960.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

7. Ilienko, V.I., Alekseev,B.P.

Dynamics of the poliomyelits virus propagation in the intestines of children immunized with attenuated live vaccine

Live vaccine against poliomyelitis,L.,1960.

8.Ilienko,V.I.,Kurnosova,L.M.,Zhidova,G.P.,Radionova,R.N.

Materials on the virusological and serological examination of children contacting subjects immunized with attenuated live vaccine against poliomyelitis

Live vaccine against poliomyelitis,L.,1960.

9.Kantorovich,R.A., Zhilova,G.P.,Ostrovsky,G.D.,Rykushina,B.P. Bregantseva,P.V.,Golubeva,L.P.

Experience with mass immunization of children in the Pskov and Novgorod regions with attenuated live vaccine against poliomyelitis

Live vaccine against poliomyelitis,L.,1960.

10.Kardash,I.B.,Votyakov,V.I.,Ilienko,V.I.,Monakhova,O.I.,Selivanov,Ya.m.,Feldman,E.V.,Bondareva,N.V.,Mar,G.I.,Sheremetieva,L.G.

The study of epidemiological efficacy of attenuated live vaccine in the Bielorussina SSR.

Live vaccine against poliomyelitis,L.,1960.

11. Kosmachevsky,V.V., Glazkova,G.S.,Aleksandrova,V.P.

Clinical observations over children of pre=school age immunized enterally with live vaccine against poliomyelitis.

Live vaccine against poliomyelitis,L.,1960.

12. Kurnosova,L.M.,Zhilova,G.P.

Immunological changes in the blood of children immunized with live vaccine against poliomyelitis.

Live vaccine against poliomyelitis,L.,1960.

13. Smorodintsev,A.A.

Theoretical backgrounds for the use of live vaccine

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

against poliomyelitis.

Live vaccine against poliomyelitis,L.,1960.

14. Smorodintsev,A.A.

Methodical directions with respect to the organization and realization of peroral immunization with attenuated live vaccine against poliomyelitis.

Live vaccine against poliomyelitis,L.,1960.

15. Smorodintsev andcollaborators,

Live vaccine against poliomyelitis.

Year=book of t. Institute of the Experimental Medicine for 1957, 301-315,1958.

16. Smorodintsev,A.A. and collaborators.,

Live vaccine against poliomyelitis.

Current problems of immunology,192-309,1959

17. Chumakov,M.P and coll.,

Preliminary communication on the mass peroral immunization of the population against poliomyelitis with live vaccine prepared from attenuated A.Sabin's strains.

18. Chumakov,M.P. and coll.,

Comparative characteristic features of the live vaccine against poliomyelitis.

Problems of virusology,No.5,533-537,1959.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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T.I

THE NUMBERS OF VACCINATED AND OF CONTROL GROUPS IN THE BIELORUSSIAN, LATVIAN, MOLDAVIAN SSR, NOVGOROD AND PSKOV REGIONS IN 1959

Districts	Age-groups	Subjects in the groups under observations		
		Vaccinated	Internal control	External control
Bielorussian SSR	6 mon.-3 yr.	74868	77612	344076
	3 yr.- 7 yr.	119897	152353	614350
	7 yr.-14 yr.	347754	85371	977375
Total		542519	315336	1 935 801
Moldavian SSR	9 mon.-3 yr.	72274	52366	107277
	3 yr.- 7 yr.	80551	42481	109500
	7 yr.-14 yr.	201782	26826	164857
Total		354 607	121 673	381 634
Latvian SSR	9 mon.-3 yr.	27840	56065	32103
	3 yr.- 7 yr.	55349	32752	35744
	7 yr.-14 yr.	159751	18055	73488
	14 yr.-30 yr.	178604		
Total		421544	106872	141 335
Pskov region	9 mon.-3 yr.	49292	7133	-
	3 yr.- 7 yr.	45699	6526	-
	7 yr.-15 yr.	102843	21594	-
Total		197 834	35 253	-
Novgorod region	9 mon.-3 yr.	41438	6979	-
	3 yr.- 7 yr.	39990	3970	-
	7 yr.-15 yr.	80341	13875	-
Total		161 769	24 824	-
Grand total		1 677 273	603 958	2 458 770

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T.2

IMMUNOLOGICAL PATTERN OF THE UNDER-AGED POPULATION OF LENINGRAD, NOVGOROD REGION, LATVIAN SSR AND MOLDAVIAN SSR WITH RESPECT TO THE POLIOMYELITIS VIRUS OF VARIOUS TYPES

Age-Groups	I type % of negatives					II type % of negatives					III type % of negative					% of triply negative				
	Leningrad	Novgorod Region	Latvian SSR	Moldavian SSR	Belorussian SSR	Leningrad	Novgorod Region	Latvian SSR	Moldavian SSR	Belorussian SSR	Leningrad	Novgorod Region	Latvian SSR	Moldavian SSR	Belorussian SSR	Leningrad	Novgorod Region	Latvian SSR	Moldavian SSR	Belorussian SSR
0 - 2	77	63	64	64	60	72	87	78	79,2	65	64	82	66	64,4	65	48	48	41	33,6	36
3 - 4	41	31	42	28	45	41	60	50	37,9	54	48	47	35	36,7	50	28	15	20	9,1	22
5 - 6	28	18	25	20	40	38	46	41	25	53	37	35	23	29	26	18	6	6	5	0
7 - 9	29	18	25	20	31	26	42	39	26	37	29	33	29	26	33	14	6	4	4	13
10 - 12	26	11	19	15	35	26	33	34	23	50	37	30	27	22	27	7	4	0	3	20

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SUSCEPTIBILITY TO POLIOMYELITIS OF CHILDREN AND ADOLESCENTS IN THE LATVIAN SSR BEFORE AND 6 MONTHS AFTER TWOFOLD IMMUNIZATION WITH LIVE VACCINE

The age of the examined (years)			Before Vaccination: Number of examined	Before Vaccination: % of subjects with no antibodies to poliomyelitis virus: I type	II type	III type	All the three types	After vaccination: Number of examined	After vaccination: % of subjects with no antibodies to poliomyelitis virus: I type	II type	III type	All the three types
0	–	2	55	60	65	55	36	68	19	11,7	19	1,5
3	–	4	22	45	54	50	22	49	8	6,1	8	2
5	–	6	15	40	53	26	0	67	1,5	1,5	4,5	0
7	–	9	45	51	37	33	12	60	1,5	16,6	10	1,6
10	–	12	48	35	50	27	20	51	11,7	11,7	18	0
13	–	15	35	28	31	17	0	31	9,7	8,2	3,2	0
Total			220					326				

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SUSCEPTIBILITY TO POLIOMYELITIS OF CHILDREN IN THE BIELORUSSIAN SSR BEFORE VACCINATION AND 6 MONTHS AFTER TWOFOLD IMMUNIZA TION WITH LIVE VACCINE

The age of examined (years)	Before vaccination					After vaccination				
	Number of examined	% of subjects with no antibodies to poliom. virus				Number of examined	% of subjects with no antibodies to poliomyelitis virus			
		I type	II type	III type	all 3 types		I type	II type	III type	All three types
0-2	67	64	78	66	41	33	0	9	3	0
3-4	45	43	50	35	20	30	10	13	13	0
5-6	44	25	41	23	6	41	10	4,8	22	0
7-9	72	25	39	29	4	67	1,5	1.5	12	0
10-12	43	19	34	27	0	84	3,5	4,7	14	0
13-15	25	16	22	4	0	78	1,2	1	5	0
16-20	22	18	18	10	0	56	9	5,3	16	0
total	406	1				389				

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SEASONAL DYNAMICS OF PARALYTIC POLIOMYELITIS INCIDENCE IN BYELORUSSIA, LATVIA AND MOLDAVIA DURING 1957-1959 IN AREAS COVERED (+) AND NOT COVERED (-) BY VACCINATION IN 1959.

REPUBLICS	Years	Areas covered by immunisation in 1959	Months of the year: January	February	March	April	May	June	July	August	September	October	November	December	Total
Byelorussia	1957	-	6 6	6 8	3 5	4 5	4 6	14 21	20 59	30 58	29 43	25 33	6 18	18 24	161 286
	1958	-	11 20	6 10	14 26	6 18	15 13	21 45	62 49	48 58	47 82	35 51	16 51	9 20	288 413
	1959	-	9 8	5 14	5 3	5 12	14 17	9 12	5 19	8 20	6 19	6 11	6 8	1 7	77 135
Latvia	1957	-	11 2	5 -	4 1	2 2	3 -	2 3	6 1	9 4	14 2	13 -	3 -	2 2	72 17
	1958	-	- 2	3 1	1 -	2 -	2 -	8 2	17 3	28 6	18 6	22 1	17 6	10 3	123 30
	1959	-	4 -	2 1	5 -	1 -	- -	1 3	- 6	2 3	- 1	1 2	- -	- -	16 14
Moldavia	1957	-	0 0	0 3	0 0	1 2	0 2	0 1	0 2	0 16	3 25	7 11	8 2	7 2	26 63
	1958	+	1 7	5 17	3 33	3 14	7 3	27 23	30 19	16 22	28 17	14 4	5 0	3 2	140 131
	1959	-	4 5	5 1	2 7	3 1	1 1	4 5	1 4	2 11	0 10	1 13	1 3	1 1	25 62

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T.3

THE NUMBER OF PARALYTIC CASES OCCURRING DURING THE EPIDEMIC SEASON OF 1959 IN THE AREAS OF BIELORUSSIA, LATVIA AND MOLDAVIA COVERED AND NOT COVERED BY IMMUNIZATION

Republic	Age-groups	Non-vaccinated (external control)			non-vaccinated (external control)			Population Census	Immunized with live vaccine		The number of anticipated poliomyelitis cases
		Census of population	No. of cases Total	Convent. index per 100 000 of inhabitants	Population census	No. of cases Total	Conventional index per 100 000 of popul.		No. of cases Total	Conventional index per 100 000 of popul.	
Bielorussia	6 m.- 3 yr.	344076	82	5,7	77612	35	67,3	74868	2	4,0	33
	4 yr.-7 yr.	614350	23	5,6	152353	10	9,9	149897	3	3,7	7
	8 yr.-14 yr.	977375	12	1,8	85371	2	3,5	347754	1	0,4	8
	Total	1935901	117	9,4	315336	47	22,0	542519	6	1,6	48
Moldavia	9 m.- 3 yr.	79066	36	78,2	37744	7	31,8	72274	2	4,1	36
	4 yr.-7 yr.	66886	4	10,5	26870	0	0	80551	0	0	3
	8 yr.-14 yr.	164857	1	1,0	24239	0	0	201782	0	0	0
	0-7 yr.(immunized with Salk vaccine)	70825	6	14,7	32820	1	5,1				
	Total	381634	47	21,9	121673	8	6,5	354607	2	0,8	39
Latvia	9 m. -3 yr.	32103	1	5,2	36055	2	7,1	27840	0	0	1
	3 yr.-7 yr.	35744	3	16,8	32752	0	0	55349	0	0	4
	7 yr.-14 yr.	73488	5	13,6	18055	0	0	159731	1	1,2	10
	Total	141335	9	12,8	106872	2	3,9	242940	1	0,8	15

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ANALYSIS OF POLIOMYELITIS INCIDENCE IN BYELORUSSIA DURING 8 MONTHS OF 1959

T.7

	Age-groups	Number of children in age-groups	Percent	Number of poliomyelitis cases by months: May	June	July	August	September	October	November	December	Total for 8 months	Mean annual index per 100,000 children	Expected number of cases
Immunized with live vaccine	6 mo.-3 yr.	74868	13.8	-	-	-	1	-	-	-	-	2	4.0	33
	4 yr.-7 yr.	119897	22.1	-	-	-	-	1	2	-	-	3	3.7	7
	8 yr.-14 yr.	347754	64.1	-	-	-	-	1	-	-	-	1	0.4	8
	Total	542519	100	1	-	-	1	2	2	-	-	6	1.3	48
Non-vaccinated (internal control)	6 mo.-3 yr.	77612	24.6	10	4	3	6	4	4	3	1	35	37.8	
	4 yr.- 7 yr.	153853	48.8	1	5	2	1	-	-	1	-	10	9.9	
	8 yr.-14 yr.	85371	27.1	-	-	-	-	-	-	2	-	2	3.5	
	Total	315836	100	11	9	5	7	4	4	6	1	47	22.0	
Non-vaccinated (external control)	6 mo.-3 yr.	344076	17.7	13	8	17	14	4	7	4	5	82	35.7	
	4 yr.-7 yr.	614330	31.7	3	3	3	4	4	2	2	2	23	5.5	
	8 yr.-14 yr	977375	50.4	1	1	-	2	1	2	5	-	12	1.8	
	Total	1935801	100	17	12	20	20	19	11	11	7	117	9.0	

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DISTRIBUTION OF PARALYTIC POLIOMYELITIC CASES IN JUNE–DECEMBER 1959 ACCORDING TO THE TERRITORIES COVERED AND NOT COVERED BY IMMUNIZATION WITH LIVE VACCINE IN THE MOLDAVIAN SSR

T.8

Groups	Kind of vaccination	A g e	Numerical composition of groups	%	The number of paralitic VII	VIII	IX	X	XI	XII	Total	Conventional index in estimating per 100 000 p.	Number of anticipated cases
I	Immunized with live vaccine	9 m.–3 yr.	72274	20,4	–	–	2	–	–	–	2	4,1	36
		3yr.–7 yr.	80551	22,7	–	–	–	–	–	–	–	–	3
		7yr.–14yr	201782	56,9	–	–	–	–	–	–	–	–	–
Total			354607	100,0	–	–	2	–	–	–	2	0,8	39
II	Immunized with Salk vaccine (triple)	9 m.–3 yr.	14622	12,0	I	–	–	–	–	–	I	11,6	
		3yr.–7 yr.	15611	12,8	–	–	–	–	–	–	–	–	
		7yr.–14yr.	2587	2,0	–	–	–	–	–	–	–	–	
		Total	32820	25,8	I	–	–	–	–	–	I	3,1	
III	non-vaccinated (internal control)	9 m.– 3yr.	37744	31,1	3	I	–	I	I	I	7	31,8	
		3yr.– 7yr	26870	22,2	–	–	–	–	–	–	–	–	
		7 yr.–14yr	24239	19,9	–	–	–	–	–	–	–	–	
		Total	88853	73,2	3	I	–	I	I	I	7	13,5	
	Total		121673	100,0	4	I	–	I	I	I	8	10,7	
IV	Non-vaccinated external control)	9 m.– 3yr.	79066	20,7	4	2	9	10	I	I	36	78,2	
		3yr.–7yr.	66886	17,3	I	I	I	I	–	–	4	10,5	
		7yr. –14yr	164857	43,4	–	–	–	–	I	–	I	1,0	
		Total	310809	81,4	5	2	10	11	2	I	41	22,5	
V	Immunized with Salk vaccine	9 m.– 3yr.	28211	7,4	–	–	I	2	–	–	3	18,0	
		3yr.– 7yr.	42614	11,2	–	I	–	–	I	–	3	11,8	
		7yr.–14yr.	0	0	–	–	–	–	–	–	–	–	
		Total	70825	18,6	–	I	2	2	I	–	6	14,7	
Global			381634	100,0	5	3	12	13	3	I	47	21,9	

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STAT

MATERIALS ON IMMUNOLOGICAL AND EPIDEMIOLOGICAL EFFICACY OF LIVE VACCINE AGAINST POLIOMYELITIS

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The large=scale use in recent years of Salk killed vaccine to control poliomyelitis has not eliminated the threat of acute anterior poliomyelitis developing in triply incoculated children and has failed to influence the virus circulation in childrens' establishments. Restricted duration of the post=vaccinal immunity required repeated immunization following a completed cycle of triple inoculations with the killed vaccine.

The necessity to sacrifice vast numbers of monkeys to prepare each and every million doses of killed vaccine has already become a source of considerable difficulties in securing the needed stock of monkeys for the ever=increasing production of this preparation.

At present the large=scale output of a complex, costly and insufficiently effective Salk vaccine, which necessitates inflicting additional traumas to children by repeated injections, can be entirely dispensed with in view of the possible complete replacement of the killed vaccine with a more effective, fully harmless, maximally convenient and accessible live one, administered perorally and prepared from the A.Sabin or G.Koprovsky strains /13/.

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STAT

The vaccination of the Polish population with the living Polio vaccine

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From the Department of Virology of the State Institute of Hygiene, Warsaw

/Provisional Communication/

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In 1959 studies on the living attenuated vaccine, prepared from the Koprowski's strain /type 1/ have been completed. Vaccination has been performed in a small town and three adjacent villages with a total population of 716. In all 2 888 persons - aged 6 months to 16 years - have been vaccinated e.i. 95% of the registered population in this age group. No complications have been observed among the vaccinated, instead the increase of the antibody level after vaccination has been seen. The vaccination campaign was inaugurated on October the 20th 1958 and since then during 18 months no case of Polio has been registered in these localities.

On the basis of the studies named above, the Ministry of Health appointed a special Committee which recommended the inauguration of a mass vaccination campaign on the following conditions.

1/ Children aged 6 months to 7 years should be vaccinated with the inactivated Salk's vaccine at least twice, before the inoculation of the living virus can take place.

2/ Children over 7 years of age, may be vaccinated with the living vaccine, without the previous administration of the Salk s vaccine.

On the basis of these recommendations a plan of the vaccination campaign with the living vaccine has been worked out. The menagement of the campaign was entrusted to the Sanitary Epidemiological Stations /Each province - województwo - is provided with a station/. The vaccines -

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type 1 and 3 - were supplied by Dr. H.Koprowski. The vaccines have been studied by the Department of Virology of the State Institute of Hygiene before the vaccination campaign in the following directions:

1/ the determination of $TCID_{50}$

2/ the investigation of the neuropathagenic properties of the strains in question, for monkeys;

3/ the trial of the vaccine on small groups of children in order to establish the dose to be inoculated

ad 1/ $TCID_{50}$ type 1 was equal to the $\log.10^{-6,95}$, that for the type 3 - $\log.10^{-7,3}$;

ad 2/ The vaccine of the type 1 /CHAT 18 GI/ was inoculated intercerebrally to 53 monkeys; no clinical symptoms were observed, however in two cases histopathological lesions could be certified. The same vaccine was inoculated intervertebrally to 24 monkeys: in 7 cases definite clinical symptoms could be ascertained, in 10 monkeys histopathological lesions could be established /44%/.

Table Nr 1

Table Nr 2

The vaccine type 3 /Fox/ was inoculated to 19 monkeys. No clinical symptoms manifested themselves. On the other hand there were ascertained atypical histopathological lesions in one monkey, and typical in a second one.

30 monkeys received an intervertebral injection of the same vaccine. Out of this total typical clinical symptoms

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were observed in three cases, douptful in four, and histo-pathological lesions in 9 monkeys - 30%.

Table Nr 3

Table Nr 4

ad 3/ Studies have also been made on children in order to determine the dose which could be applied during vaccination. The investigation has been made in a Home for children. The number of children vaccinated amounted to 37. Different doses were used.

In the beginning the strain type 1 was used - this procedure was followed by the inoculation of the type 3, after a monthly interval. The results of this experiment will be discussed separately.

The vaccination campaign was inaugurated on October the 20th, and ended on March the 3nd 1960. For the type 3 the campaign will be concluded by April the 15th /1960/.

The vaccination campaign lasted usually from 6 to 12th say in each province. It was carried out in separate provinces /województwa/ on fixed dates.

M e t h o d s o f a d m i n i s t r a t i o n o f t h e v a c c i n a t i o n c a m p a i g n. On fixed dates the vaccine was dispatched by car to different provinces. It was stored in containers with dry ice. The ampoules contained 1 or 2 ml. of vaccine. The instruction provided that the dilution of the vaccine in the physiological saline solution shall be performed at the laboratories of the Provincials Epidemiological Stations. For the type 1 the dilu-

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tion must correspond to 1/500 i.e. 200 000 infective doses /$TCID_{50}$/, and for the type 3 - 1/1000 i.e. about 1000 000 infective doses /$TCID_{50}$/. After this procedure the diluted vaccine was placed in containers with ordinary ice and delivered by car to the vaccination points. It could be administered a few hours after dilution. During the whole period of the vaccination campaign, the vaccine was stored in refrigerators, or on ice. The instruction directs that the diluted vaccine may be used for inoculation during the first 48 hours after dilution, only. Samples of the diluted vaccine were collected at vaccination points and the titer of the virus examined in a laboratory. In all, 8 samples were examined, and in all these cases satisfactory results were obtained.

The dosage prescribed and administered orally to the children was 1 ml. Such on amount was added to 4 ml. of distilled water with 10% glucose.

The percentage of vaccinated varies in different provinces from 63 to 99%. 7 129 874 persons were vaccinated with type 1 i.e. 83,5% of registered children in the age group 6 months to 15 years.

Map Nr 1

Up to March the 25th 4 918 137 persons were inoculated with type 3. In some of the provinces the vaccination campaign is - as yet - not finished.

Map Nr 2

It should be added that in these provinces in which type 3 was used for vaccination the percentage of persons

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applying for vaccination varied from 84 to 98%.

At present virusological and serological examinations of the vaccinated is made in 6 provinces. The work will be finished by the middle of the current year.

It is difficult to evaluate at present the results of the vaccination campaign, as only virusological, serological and epidemiological studies may give a definite answer.

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Table Nr 1

Studies of the living Polio vaccine type 1 on monkeys

Intercerebral injections

Date	Series	Clinical	Histopathological
20.V	WCH 18	0/5	0/5
8.IX	WCH 18 GI	0/14	2/14
12.X	WCH 18 GI	0/25 x/	0/25
24.X	WCH 18 GI	0/9	0/9
	T o t a l	0/53	2/53

x/ The different dilutions 10^{0}, 10^{-1}, 10^{-2}, 10^{-3}, 10^{-4} of the vaccine injected intracerebraly. Each dilution was injected to 5 monkeys.

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Table Nr 2

Studie of the living Polio vaccine type 1 on monkeys

Intraspinal injections

Date	Series	10^0		10^{-1}		10^{-2}	
		Cl.	Hist-poth	Cl.	Hist-poth	Cl.	Hist-poth
30.V	WCH 18	2/9	3/9	4/10	5/10		
24.X	WCH 18 GI					1/5	2/5
	T o t a l	2/9	3/9	4/10	5/10	1/5	2/5

The total number of inoculated monkeys 24

Symptoms 7

Histopathological changes 10 = 44%

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Table Nr 3

Studies of the living Polio vaccine W F X on monkeys

Intercerebral injections

Date	Series	10^0		10^{-1}	
		Clinical	Histopathological	Clinical	Histopathological
18.IX	WF X	0/9	1+ / /0/9		
4.XI	WF X	0/5	0/5	0/5	1/5
	Total	0/4	1+ / / 0/14	0/5	1/5

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Table Nr 4

Studies of the living Polio vaccine type 3 on monleys

Intraspinal injections

Date	Series	10^0		10^{-1}		10^{-2}		10^{-3}	
		Clinical	Histopath.	Clinical	Hist.	Clin.	Hist.	Clin.	Hist.
18.IX	WF X	2/ /+2/5	2/5	2/ /+0/5	0/5				
4.XI	WF X	0/5	2/5	1/5	3/5	1/5	1/5	0/5	1/5
	Total	2/ /+2/10	4/10	2/ /+1/10	3/10	1/5	1/5	0/5	1/5

Total number of monkeys examined	30
Douptful clinical symptoms	4
Typical clinical symptoms	3
Histopathological changes	9 = 33,0%

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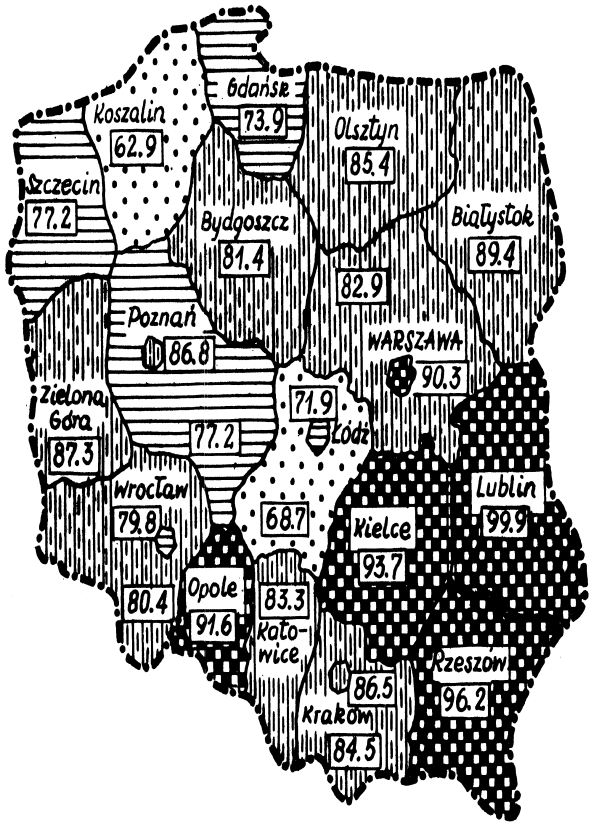
MAP N. 1.

Poliomyelitis voccination with Koprowski oral voccine type I, in Poland population in age 6 month – 15 years.
Percentoge vaccinated in each province.



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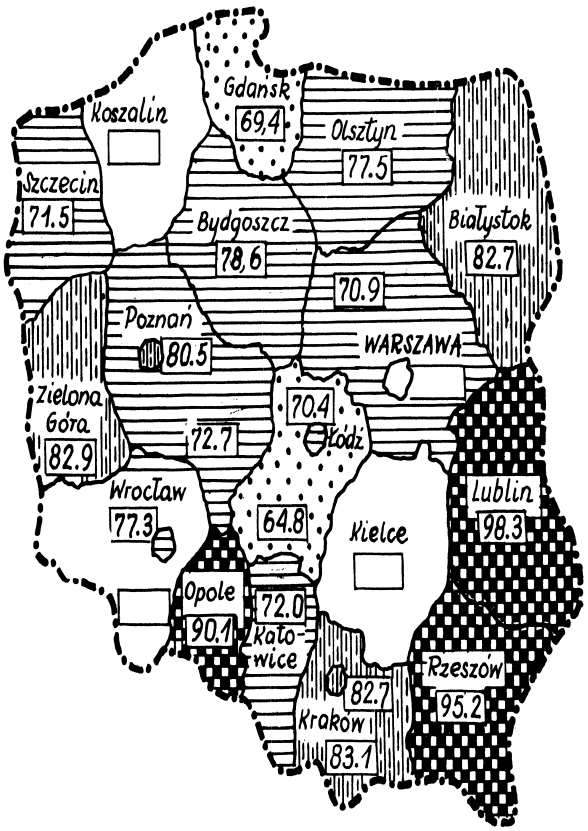
MAP N. 2.

Poliomyelitis voccination with Koprowski oral voccine type III, in Poland population in age 6 month – 15 years.
Percentoge vaccinated in eath province.



60-70% 70-80% 80-90% 90-100%

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Vaccination against poliomyelitis with live Sabin vaccine in Hungary

(Preliminary report)

By

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O. Rudnay and D. Boda

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I. The epidemiology of poliomyelitis in Hungary

Since 1954 the number of poliomyelitis cases has greatly increased in Hungary. Formerly, poliomyelitis epidemics occured only in 1931 with 1138 reported cases and in 1947 with 1035 cases. This corresponds to a morbidity of 13.1 and 11.4, respectively for 100,000, while in the non epidemic years the incidence of poliomyelitis was between 1.3 to 6.2 for 100,000. In 1954 and 1956 the number of poliomyelitis cases was 1176 and 1100, respectively, and in 1957 the following year, an exceptionally severe epidemic took place with 2334 cases, corresponding to a morbidity of 23.8 $^{0}/_{0000}$. The year 1958 was free of epidemic with only 165 cases, with a morbidity of 1.7 $^{0}/_{0000}$. A serious epidemic took place in 1959 with 1830 cases, with 18.3 $^{0}/_{0000}$ incidence rate. Fig. 1 shows the curve of poliomyelitis morbidity between 1945 and 1959.

In the 1957 epidemic the morbidity started to increase in May and reached its peak in July. In 1959 the number of cases started to increase in June, reaching a maximum in August, as shown in Fig. 2.

Virus isolations have shown that both the 1957 and 1959 epidemics were caused by type I poliovirus. Thus, out of the 430 clinical cases of poliomyelitis in 1959, we isolated type 1 in 343 cases. Type II ans III strains were found in 2 and 8 cases respectively though either before or after the epidemic only. From patients suspicious for poliomyelitis, type I virus was isolated in 131 and type III in seven cases. In addition, type I poliovirus was isolated in 25 cases of meningitis serosa and in 15 cases of facial paraesis.

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II. Salk vaccinations in Hungary

The severe epidemic in 1957 urged the introduction of preventive vaccinations already during the epidemic. From the 18th of July, 1957 to the end of the same year, 80 per cent of children between the ages of six months to six years, i.e. a total of 927,552 children, received two intracuteneous dosis with an interval of four weeks. Out of the children over six years of age, 271,675 received two doses of Salk vaccine. Large scale Salk vaccinations were carried out in Hungary in 1958, when children between the ages of six months and eighteen years received three doses of vaccine intramuscularly. A total of 2,134,589 children representive 70 per cent of the above age group were vaccinated. In 1959, 120,000 children between the ages of six and 18 months received two intramuscular doses prior to the epidemics in March and April, and a third one in July and August. Another 282,727 who missed vaccination in the previous year were vaccinated in July and August while 304,913 children received a fourth dose.

As a result of the Salk vaccinations carried out in the years 1957, 1958 and 1959, the 90 per cent of the population under 18 years of age were vaccinated three times.

The effectiveness of the Salk vaccinations will not be discussed here. The rapid decrease in the number of poliomyelitis cases, which followed the vaccinations during the 1957 epidemic suggested the favorable influence of the vaccinations. On the basis of his epidemiological studies Petrilla came to the same conclusion. The very favourable epidemiological situation in 1958 is a further proof for the effectiveness of the Salk vaccine, though the Bronholm epidemic, in the same year, could also have

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interfered with the spreading of the poliovirus. Nevertheless the outbreak of the epidemic in 1959 points to the fact that neither the immunity acquired by the 1957 epidemic, nor the large scale Salk vaccinations could not hinder a considerable increase in the number of cases and the spreading of the poliovirus to Hungary.

III. Introduction of the Sabin vaccine in Hungary

The live, attenuated poliomyelitis vaccine, as developed by Sabin and Koprovsky, offered a possibility of applying a more effective prophylactic measure instead of the inactivated Salk vaccine. Experiments were carried out in Hungary with respect to the pathogenic characteristics of Sabin strains for monkeys.

The research work carried out by Chumakov and Smarodincev on the Sabin vaccine in the Soviet Union led to important results. Thus Hungarian scientists and health authorities decided to study the possibilities of adopting this method to our country too. The Microbiological and Epidemiological Committee of the Scientific Council of the Ministry of Health suggested the introduction of the Sabin vaccine in Hungary, in July 1959.

Although the original plan envisaged only small scale vaccinations for 1959 and a general introduction of the vaccine was planned for 1960, the serious epidemiological situation made it necessary to carry out the vaccinations earlier than originally contemplated.

To the Microbiological Congress held in Budapest, in September, 1959, dr Sabin sent the lecture and Professor Chumakov and dr. Skovranek reported on their work carried out in the Soviet Union and Czechoslovakia, respectively. These reports served as a final basis for the use of the Sabin vaccine in Hungary. The co-

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operation which developed between the representatives of the three countries with respect to this question at the Congress, deserves to be specially mentioned. Chumakov offered the help of the Soviet Union in sending us vaccine prepared and widely used in their country and in putting to Hungary's disposal all informations concerning the production of the vaccine. Dr. Kátay, Fornosi and D. Boda had an opportunity to study the production and administration of the vaccine in Moscow. The Ministry of Health elaborated a plan for vaccination of children between the ages of three months and 14 years with Sabin vaccine. Vaccination was carried out in two steps:

In step one in November, 1959, 96,852 children were vaccinated in Gyor-Sopron County with trivalent vaccine and revaccinated one month later.

In the second step children of the same age group in the rest of the country were vaccinated.

These 2,403,761 children received three doses of monovalent vaccine at one month intervals: type 1 in December, 1959, then type 3 in January 1960 and finally type 2 in February of the same year. The monovalent vaccines received from Professor Chumakov had a titre of log 7 to log 7.5. The content of 1 ml ampoules was diluted to 10 mls by solvent (Hanks) at the place of vaccination. One dose of vaccine contained 100,000 to 200,000 CPD 50 of virus, in two drops of liquid which was given to the younger children in tea and to the older ones on sugar. Vaccination was compulsory for the age groups between three months and two years, but all children not attending a nursery, kinder-garten or school were invited to the vaccination centres on the basis of lists compiled by the district general practioners, while the nurseries, kinder-gartens and schools provided for collective vaccination

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of the children. Important preparatory work was carried out by the Ministry of Health which issued detailed instructions on the tr theoretical and practical aspects of their task to the County Chief Health Officers, Hospital Directors and epidemiologists. These again prepared the health organizations of their county, district or town for the performance of the task ahead. Large scale enlightening and organizational work was carried out with the help of the social organizations, first of all of the Red Cross. The national and local press and the Radio participated in this work too.

The vaccination program was started with the administration of trivalent vaccine in County Gyor-Sopron with 392,000 inhabitants. Vaccination was carried out between the 3-5. November and revaccination with the same vaccine between 17-21 December. As already mentioned, the number of poliomyelitis cases was exceptionally high in County Gyor-Sopron during 1959. There were 44 cases in August, 29 in September, 10 in October and - prior to the beginning of the vaccinations - 4 in the first days of November. 96,852 children received the first and 98,184 the second vaccination, which amounts to more than 96 per cent of the age group for which vaccination was compulsory.

2,403,761 children were vaccinated with monovalent type I vaccine. About 92 per cent of children belonging to the age group between three months and 14 years were vaccinated. 234,438 persons above the age of 14 were also vaccinated. Vaccination with type III was carried out on the 21-22-nd January, 1960. A total of 2,474,422 children and adults were vaccinated, more than with type I. 273,536 were over 14 years of age. Table I shows the number of people vaccinated. Vaccination with type II was carried

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out between 23-27 th February. No exact data concerning the number of people vaccinated was available up to the 17th March, but the participation was apparently as active everywhere as during previous vaccinations.

Those who either were left out during the previous vaccination for some reason (intercurrent illness) or have not yet reached the age of three months then or were born since are going to be vaccinated in May this year. We have also in mind to deal with the problem of buster vaccinations.

IV. Safety and effectiveness of the Sabin vaccine

We considered the question of safety and effectiveness of the Sabin vaccine as settled already prior to starting the vaccinations. This authorised us to carry out such a large scale vaccination program within such a short time. Nevertheless, it was most important that both the doctors and the public should be convinced about the safety of the Sabin vaccine. Furthermore, it was also important to study whether the reactions of the organism induced by the Sabin vaccine are entirely free of clinical symptoms. In the Laszlo Hospital, Budapest (central hospital for infectious diseases) all children hospitalised for various reasons and having a normal temperature were vaccinated at the time of the national program. These children could be kept under careful clinical observation. 688 children were vaccinated with type I, 520 with type III and 563 with type II. No increase of temperature, intestinal or neurological symptoms could be observed in these children after vaccination.

Another 30 children were treated for various reasons with cortisone in the same hospital. It is a known fact that cortisone

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reduces the resistance of the organism to infectious diseases. These 30 children had also received the Sabin vaccine which, in spite of the cortisone treatment, caused no clinical symptoms whatsoever.

No conclusions can naturally be drawn as to the effectiveness of the Sabin vaccine four months after the County Gyor-Sopron and three months after the beginning of the nation wide vaccination campaign. It is, however, important to study the poliomyelitis cases occurring after the vaccination. The conditions were specially favourable in County Gyor-Sopron, in Budapest and in County Pest, as all children suspected for having poliomyelitis were hospitalised in the László Hospital where facilities for the most careful and correct observation and diagnosis have been available. No case of poliomyelitis occurred in County Gyor-Sopron for the last four and a half months, since 3d November, 1959. In Budapest and County Pest, with a total of 2,589,000 inhabitants, vaccination with monovalent vaccines was started on 15th December; since that time no case of poliomyelitis has been reported from this area. Thus no case of poliomyelitis occurred among 2,981,000 persons vaccinated in these areas, i.e. in an area where about a 30 per cent of the total population of Hungary is living. Nevertheless only a few cases of poliomyelitis have been reported from other areas of the country either. These data, however, require further thorough investigation as clinical and virological examinations revealed in more than one case that the first diagnosis was incorrect. It seemed, however, remarkable that in the Counties Cyor-Sopron and Pest and in Budapest, where 648 poliomyelitis cases had been reported between July and October, 1959, no

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further cases of poliomyelitis were observed after the accomplishment of the vaccination program.

Vi Examination of virus excretion

The examination of virus excretion was carried out on the basis of a carefully projected plan by Drs Dömök and Molnar in the Virus Department, led by Dr. E. Farkas, of the State Institute of Hygiene, Budapest. These examinations were performed to determine 1/. The incidence of wild poliovirus strains among healthy chi'dren prior to the vaccination, 2/ the excretion of vaccine strains after vaccination and in case of vaccination with a trivalent vaccine, the possible interference of the different vaccine strains with each other in the human organism. In connection with the vaccination in County Gyor-Sopron 160 children, belonging to various age groups, have been examined as to their virus excretion. Fecal samples were taken from the children on three consecutive days prior to the vaccination and on the third, fifth, 12th, 14th, 22nd and 25th day after the vaccination. Only one individual was examined from each community. Samples collected over several days were used for each examination. Virus isolations were carried out on monkey-kidney-tissuescultures and tests for Coxsackie "A" virus on suckling mice.

Examination of the virus excretion prior to vaccination revealed following results: out of 160 children 52 excreted one or other enteral virus (32.5%). Twenty-five children excreted poliovirus, out of them 14 type I and 11 type III. Seventeen children excreted ECHO virus, two Coxsackie "B" and eight Coxsaclie "A". These results show that at the end of the 1959 epidemic, poliovirus infestation was still very high in County Gyor-Sopron

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(15.6%). The relatively high incidence of type III poliovirus seemed to be of certain interest. As to the other enternal viruses the excretion of ECHO virus was rather frequently observed. Three to five days after vaccination 122 children excreted virus (77% of those examined). Type I poliovirus was isolated from 32 children, type II from 74 and type III from 82.

Twelve to fifteen days after vaccination the number of excretors dropped to 98 (63%).

Twenty-two to twenty-five days after vaccination the number of children excreting virus dropped to 77 out of the 152 examined (51%). Out of them only three excreted viruses other than poliovirus, compared to 29 prior to vaccination. Twenty-three excreted type I poliovirus, 24 type II and 51 type III. The reselts are presented in Table II. It is noteworthy that multiplication of the type I poliovirus was rather seldom demonstrated in all the three post vaccination samples. This might be explained by the immunity resulted by the prolonged circulation of the virus following the previous severe epidemic. This supposition is supported by the 10 per cent incidence of type I virus among children prior to vaccination.

Serological examinations have also shown the presence of type I poliovirus neutralizing antibody in the sera of 93 children out of 100 from the same group, which might partly be considered as a result of past infection. It is most interesting that in the first week only 49 per cent excreted one single type of poliovirus, while 44 per cent excreted several types simultaneously. This showed that the simultaneous feeding of large quantities of different types of virus (by trivalent vaccine) did not inhibit the growth of any of three types by interference. These

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results are of considerable importance from the point of view of the effectiveness of the trivalent vaccine.

Tabel II shows the virus excretion in various age groups vaccinated with trivalent vaccine. Three repeated examinations failed to prove the presence of any virus in 24 children out of 151, while 125 (83 per cent) excreted poliovirus.The first age group of children between the ages of two months and four years included 70 children out of whom 65 excreted poliovirus (93 per cent). In the age group five to fifteen years 60 out of the 81 children (74 per cent) excreted poliovirus after vaccination. Virus excretion by the younger age group also shows that this age group was less infected by poliomyelitis than the age group from five to fifteen years in whom the vaccine strains did not grow in the intestinal tract owing to acquired immunity. The number of those excreting type I poliovirus was 53 out of 151, considerably less than the number of those excreting types II and III shiwh is a further proof to the fact that immunity to type I was much higher.

vaccination

During the nation wide Sabin program samples were collected from a total of 300 children living in the capital and in nine different counties. All children were under four years of age. From the same community only the material of one child each was sent in. Pooled fecal samples from the period before the 5-to 7 and days after the vaccination with the various types were examined respectively. These examinations are not completed as yet. Some preliminary results are presented in Tabel III.

The virological examination of the prevaccination samples shows that 15 out of 296 children excreted poliovirus and 36

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other enteral viruses. Type I poliovirus was present in 11 cases, indicating that the excretion of wild strains was very widespread in the whole country - 3.7 per cent as a consequence of the preceding epidemic, although not quite as widespread as in County Gyor-Sopron, where it was 15.6 per cent. Following vaccination with type I virus the number of excretors increased to 134, as compared to the 18 prior to vaccination out of 270 examined (50 per cent). Examinations after the second dose showed a 65 per cent excretion rate, with the highest incidence of type III virus actually fed. The above data might undergo some modifications later when the examination of the material still available will be completed.

In connection with the mass-vaccination of the child-population, large quantities of vaccine virus might have got into the sewage waters. Thus samples were taken for virological examination from the Budapest main sewage canals four to ten days after the beginning of the vaccination program. In the sample taken on December 19th we were able to prove the presence of type I poliovirus in 0.1 ml sewage water without any further concentration. This observation shows that vaccination leads to an intensive spreading of the vaccine virus which is an interesting phenomenon.

VI. Production of Sabin vaccine in Hungary

Serological studies and the relations of the Sabin vaccination to vaccinations against other infectious diseases

Simultaneously to the administration of the Sabin vaccine, the production of this vaccine was started in Hungary with an aim of using home produced vaccine in future. This work has been carried out by A. Koch in the Virus Department of the State Institute of

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Hygiene where some previous experience has been gathered about the production of Sabin vaccine. The original vaccine strains used in the production have kindly been supplied by Professor Chumakov. These strains are identical with the original Sabin strains. The production and the control of the vaccine is carried out according to the instructions given by Professors Sabin and Chumakov. We have so far produced 25 litres from the three types each. Average titers of log 10^{-7} were regularly obtained. The time being the control of the vaccine is in progress. This quantity is sufficient to carry out booster vaccinations during 1960 as well as to vaccinate those who were not fed for some reasons previously. A total of two and a half million people are going to be vaccinated.

A research program concerning the problems connected with the Sabin vaccine was projected before starting the vaccination program. The Microbiological Institutes of the four Medical Universities in the country and the Virus Department of the State Institute of Hygiene, Budapest agreed in examining special points of the problem each. Virus excretion examinations, as described in par. VI, have been carried out within the framework of this research program. Serological tests showed the development of immunity following the administration of trivalent Sabin vaccine as well as the administration of the monovalent types in successive months. The State Institute of Hygiene plans the examination of 460 pairs of serum taken prior and after vaccination from the same persons on whom virus excretion tests will also be carried out. This serological work is not yet completed; dr. Fornosy will report on his results. Professor Ivánovics in Szeged and Professor Váczi in Debrecen will examine the local material from the same

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point of view. The Microbiological Institute of the Budapest and Pécs Medical Universities are studying the effect of the simultaneous administration of anti-tuberculosis vaccine (BCG) and anti-dyphteria-pertussis-tetanus vaccine with the Sabin vaccine. This problem is of great importance, as there are no data available as to the effects of simultaneous administration of Sabin and other vaccines. This work is still in progress.

The epidemiological studies have been carried out by Dr. O. Rudnai, the Salk and Sabin vaccinations were organized by Dr. A. Kátay, laboratory virological tests of the Sabin vaccine and the control of the home produced vaccine is being done by Dr. F. Fornosi, virus excretion examinations and the production of Sabin vaccine are being carried out by Drs I. Dömök, E. Molnár, and A. Koch in the Department led by Dr. E. Farkas, clinical examinations are made by Dr. Boda.

Summary

1. From November 1959 till December 1960 two and a half million children between the ages of three months and fourteen years (92 to 93 per cent of this age group) were vaccinated with live attenuated antipoliomyelitis Sabin vaccine. The vaccine was prepared in Prof. Chumakov's Institute. No unfavourable symptoms have been observed either during or following vaccination.

2. Examination of virus excretion proves that both in the trivalent and in the monovalent form the Sabin vaccine strains actively grow in most of the vaccinated persons. Owing to extensive immunity following the preceeding epidemic, no virus excretio could be found in some of the children vaccinated with Sabin vaccine. Conclusions as to the epidemiological effectiveness of

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Sabin vaccination can only be drawn after a longer period, nevertheless it seems to be noteworthy that in a carefully observed area where 30 per cent of the total population of the country lives not a single poliomyelitis case was observed among the vaccinated persons in the period following the vaccination.

3. Further vaccinations will be carried out with a vaccine produced in Hungary. Serological examinations, investigation of the problem of interference and the effect of simultaneous vaccinations with other vaccines are being carried out in five different institutes of the country.

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Some results of mass poliomyelitis vaccination with live attenuated vaccine in Estonian SSR

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Mass poliomyelitis immunization with live attenuated vaccine was carried out in Estonia in 1959 under complicated epidemiological circumstances.

Estonian SSR is a nidus of poliomyelitis of long standing. In recent years poliomyelitis cases were registered in all towns and regions of the republic. In this period poliomyelitis incidence ranged from 3.0 to 17.0 and in some years reached 24.0 per 100,000 persons (in 1958 82.4 per 100,000).

Poliomyelitis incidence in the republic involved all age-groups, with a significant number of cases being observed among adults. The number of cases in the age-group over 15 in individual years ranged from 32.6 to 46.1 per cent.

Poliomyelitis occurrence in Estonian SSR has a certain periodicity with epidemic rises every 4 or 5 years, with minimal incidence previous to the rise and gradual decline of incidence after the peak.

Marked stable seasonal prevalence of poliomyelitis has been observed. Poliomyelitis incidence during the period of seasonal rise (July-September) had a range from 4.1 to 85.2 per cent.

The last rise in poliomyelitis incidence in Estonian SSR started in 1955-1956. There was a certain decline in 1957, but since July 1958 there began marked spread of poliomyelitis assuming the form of an epidemic with a large focus in the southern part of Estonia (town of Tartu and surrounding areas).

Specific prophylaxis for poliomyelitis control was employed in 1957 in Tallinn. Salk killed vaccine was used for inoculations.

Since July 1958 vaccination of pre-school children and also of children up to 18 years of age continued. Vaccination was

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started also in the town of Tartoo, but here, however, the beginning of vaccination coincided with seasonal rise in poliomyelitis incidence. In addition to Tartoo vaccination during the outbreak was carried out also in Pyltsamaas and Elvas regions. Simultaneously vaccination was started in some regions with low incidence. A total of over 100,000 preschool children and pupils up to 18 years of age were vaccinated before the end of the year.

Under circumstances of sharply reduced poliomyelitis incidence in the focus but with continuing occurrence of poliomyelitis in adjoining regions in early January 1958 first series of poliomyelitis immunization with Sabin's original live vaccine was started. The vaccination being carried out in 14 regions of the republic was based on a "barrier principle", that is, it was done in regions surrounding the main poliomyelitis focus, and in its center (Tartu). Feedings were given to preschool children and pupils up to 18 years in institutions and living in large settlements. The vaccine was given to a total of 26,334 persons.

Mass immunization of the population of 3 months to 45 years of age began on March 15, 1959. For this program live attenuated vaccine was used prepared at the Institute for Poliomyelitis Research, the USSR Academy of Medical Sciences, and supplied for Estonian SSR by Prof. M.P. Chumakov, under whose direction both first and second series of vaccinations were done.

Feedings were mainly completed by June, 1959. A total of 694,643 persons received type I vaccine and 632,657 persons received types I, II and III vaccines, which comprises 58.0 per cent of the total population in the republic. Within the limits of individual age-groups up to 45 years 67 to 95 per cent has been vaccinated (by rough estimations). There were some varia-

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tions in age-group coverage with vaccinations in some towns and regions of the republic.

Surveillance of the vaccinees and their contacts proved complete harmlessness and areactogenicity of the live attenuated vaccine.

Vaccinations in poliomyelitis foci given to contacts of poliomyelitis patients without waiting for quarantine periods to pass indicated the effectiveness of the vaccination for under such circumstances in the environment of patients there was not a single case of poliomyelitis reported with strict follow-up of the vaccinees.

In January 1959 poliomyelitis incidence was higher than in January and December, 1958. In February the first marked tendency to reduction appeared, since May further clear reduction in incidence was observed, in subsequent months till October only individual poliomyelitis cases were reported, and since October till the end of the year there was not a single case of poliomyelitis reported in the republic.

During the period of expected seasonal rise (July-September) there was no increase in incidence; in this period only 10.0 per cent of the total annual number of cases was reported.

During the observation period, i.e. in 1959, only 59 poliomyelitis cases were reported (4.9 per 100,000 persons). Of the total number of cases there were 9 cases among the vaccinated, with 3 of them having been fed one or two times (type I and type III vaccine) and 6 having received types I, II and III attenuated live vaccine.

Attack-rate index among the vaccinated (with one feeding counted) is 1.3, among the unvaccinated 9.9 per 100,000 persons

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(calculated for the total population); the same index when calculated for the number completely vaccinated (types I, II, III vaccines) is 0.9 and for the number vaccinated only with type I or types I and III is 9.2 per 100,000 persons. Reduction in incidence among the vaccinated (calculated for the total population, with one feeding counted) is 87.8 per cent, the ratio of incidence reduction being 1:7.6.

In individual age-groups there are some variations in the coefficient of effectiveness.

Total reduction in incidence after the end of mass vaccinations (till the end of the year) compared to average for the same period in many years is 95.1 per cent, with reduction multiplicity factor 20.6 per cent.

The preliminary results of the vaccination obtained confirm the high epidemiologic effectiveness of oral live attenuated vaccine and the necessity of its use for poliomyelitis control.

It is necessary to take further measures in Estonian SSR for consolidation of the results obtained.

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Laboratory investigation of poliomyelitis cases reported in areas of mass immunization of the population in Estonian SSR with live poliovirus vaccine

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In discussion of the problems of immunization with the live poliovirus vaccine observations made in Estonian SSR are of particular interest. Combination of certain circumstances (increase of poliomyelitis incidence for many years, vaccination during winter-spring non-epidemic season, mass involvement of the population by vaccinations) helped to make most objective evaluation of epidemiologic effectiveness of vaccinations carried out in the republic in 1959 (Chumakov,1; Chumakov et al., 2).

In January-February 1959 26,000 persons in Estonian SSR (children from institutions in a number of towns and students of the University of Tartu) were vaccinated with live poliovirus vaccine. In March-June large-scale vaccination of the total population up to 50 years of age was carried out. By June 1, 1959 695 thousand persons, that is, 58.1 per cent of the total population in Estonian SSR had been vaccinated.

Estonia was the first republic of the Soviet Union where vaccination with live poliovirus vaccine was carried out as a large-scale control measure. Under the guidance of the Institute for Poliomyelitis Research, Academy of Medical Sciences, USSR, complex investigation of a number of problems concerning large-scale use of the live vaccine was organized.

For careful control of poliomyelitis incidence and thorough study of each case of poliomyelitis moving consulting team (based on Nervous Disease Clinic, University of Tartu) and special epidemiologic bureau (based on Tallinn Institute of Epidemiology, Microbiology and Hygiene) were created. Special attention was given to laboratory investigation of poliomyelitis cases in persons vaccinated with the live vaccine.

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From March 1 to June 1, 1959, during vaccinations and before the beginning of observations on epidemiologic effectiveness 13 cases were reported, of them 2 in the vaccinated and 11 in the unvaccinated. After June 1 and up to December 31, 1959 a total of 8 cases were reported, of them 7 in the vaccinated and 1 in the unvaccinated. It is quite probable that such change in the pattern of incidence before and after vaccination reflects the process of most extensive involvement by vaccinations of almost all susceptible groups of the population.

At present data are available on laboratory investigations of cases among the vaccinated. This communication is devoted to identification of these cases which is important for the evaluation of safety and effectiveness of the live vaccine in Estonian SSR in 1959.

Materials and methods

Stool specimens were collected from each patient during 3 to 4 days, as early in the disease as possible. After treatment with antibiotics (as usually) stool specimens were tested for virus isolation in monkey rhesus kidney cell cultures. In a number of cases stool specimens were simultaneously tested in human fibroblast tissue cultures and in Hep-2 cell cultures. Usually from 2 to 3 passages were done from initially inoculated cultures. Virus isolates were identified with type-specific hyperimmune sera by the cytopathogenic neutralization test in tissue culture.

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For serologic investigations paired serum specimens were collected, early in the disease and 3 to 5 weeks (sometimes later) after the onset. Serum antibody titers were determined by titrations in tissue culture cytopathogenic neutralization tests with the standard dose of the virus (100 TCD_{50}).

Poliovirus strains isolated from stools of patients were titrated at different temperatures (36° and 40°) - definition of the so-called t marker of attenuation. Methods of these tests and evaluation of strain characters were those described by Benyesh-Melnick and Melnick (3).

Results and Discussion

Table 1 presents the main results of laboratory tests with specimens from each case. Table 2 shows the results of tests with poliovirus isolates by t marker.

Observations which have been accumulated so far from different areas of the country during mass oral vaccinations allow us to state with certainty that the vaccine is completely safe and areactogenic (1,2). We consider it necessary, however, to analyse each separate case of poliomyelitis in the vaccinated in order to enlarge actual characteristics of the live vaccine.

In addition to data presented in Table 1 we shall discuss poliomyelitis cases among the vaccinated reported in 1959 in Estonian SSR.

Case 1. - Mardim, V.E., a girl of 5 (Harju district). Received one feeding of type I live vaccine, March 11, 1959.

Onset on April 2, - fever (38.5°C), pains in the right arm and right leg. Next day mild weakness of the arm and leg deve-

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loped. Two days later the temperature became normal. Six days after onset examination of the cerebro-spinal fluid revealed pleocytosis of 40 cells per cmm, protein 0.132°/oo. After two weeks in hospital muscle function completely recovered. The patient was discharged clinically well.

Stool specimen collected 18 days after the onset (April 20) yielded a type II poliovirus which is the most probable etiological agent. Tests by the t marker show the isolate to be a nonattenuated street poliovirus (see Table 2) Absence of type II antibody at 8 and 24 days after onset may be explained by a late immunologic response which is sometimes observed in poliomyelitis. Absence of type I vaccine poliovirus in stools in the absence of homologous antibody may probably be explained by interference on the part of type II street virus. We believe that this case is not associated with vaccinations because the type of the vaccine virus and that of stool isolate are different.

Case 2. - Reigo M.K., a girl of 17 years of age (Tallinn). Vaccinated on March 16 with type I, on April 16 with a mixture of types I and III and on May 21 with a mixture of all three types of the live vaccine.

Onset on May 26 - suddenly during a tennis game she felt weakness in the legs without any pains. Temperature remained normal. Neurological examination on May 29 revealed paresis of the feet (markedly weak dorsal flexion with plantar flexion present, Achilles jerks absent). After two week treatment in the hospital reflexes recovered, but weakness

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of dorsal flexion of the feet remained.

Stool specimen collected 13 days after the onset (June 8) or 18 days after vaccination yielded type I poliovirus. According to the character (absence of multiplication at 40°C) the isolated strain is the vaccine strain. It is possible that this finding of type I vaccine virus in stools only reflects the fact of vaccination and does not prove the etiologic role of the isolated strain in this case. This is confirmed by the fact that in a blood specimen taken 24 says after the onset the highest antibody titer was not to type I but to type II ($>$ 1:512), with low type III titer. We believe that this case was caused by a type II street virus which the patient had picked up before a third feeding, and, consequently, the third feeding was given during prodromal period of poliomyelitis. By the time of the third feeding excertion of type II virus ceased or it was eliminated from the intestinal tract as a result of interference with the vaccine virus, for in stool specimens collected on April 1 and 4 it was found no longer. The possibility of such interference was shown during live virus vaccination on the background of street virus circulation (Drozdov,S.G., Shirman, G.A., 4).

Discrepancy between type I vaccine virus isolation from stools and serologic evidence of type II antibody increase indicates no association of this case with vaccination, but the exact definition of the causative agent is difficult because of coincidence with vaccination period.

Case 3. - Kutjev, V.A., a boy of 2.5 years of age (Abja district). Vaccinated on April 8 with type I, May 5 with type III

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and June 10 with type II live poliovirus vaccine.

Bacame ill on June 20, with mild weakness of the right leg. Examination in the hospital on the same day revealed paresis of proximal muscle of the right leg. In the cerebrospinal fluid pleocytosis was 53 per cmm five days after the onset. Control neurological examination at 16 days showed the neurologic status to be normal. 30 days after the onset the cerebro-spinal fluid contained 3 cells per cmm, protein 0.22 °/oo. Complete clinical recovery.

Stool specimen collected 18 days after the onset yielded no virus. Serologic examination 11 and 18 days after the onset revealed rise of antibody titers both to type II and type III polioviruses. In this case paralytic infection is likely to be caused by type III street virus picked up after the third feeding or shortly before it, because 45 days after type III feeding (or the 10th day of illness) type III antibody titer was 1:8, but a week later increased more than 2-fold. This indicates a recent infection (late after vaccination) and paralysis to be caused by type III street virus. Analysis of these circumstances confirms that this case was not associated with vaccine feedings.

Case 4. - Märja, K.V., a girl of 16 years (Tallinn). Vaccinated on March 17 with type I, April 16 with a mixture of types I and III and May 7 with a mixture of all three types of vaccine viruses.

Became ill two months after vaccine feedings. On July 6 she felt weakness in the right leg, but contunued working till July 25. Hospitalized on July 27. Neurologic examination

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showed weakness of dorsal flexion of the right foot. At 22 days after the onset the cerebrospical fluid contained 5 cells per cmm, protein 0.1°/oo. Discharged practically well.

Stool specimen, collected 29 days after the onset yielded a strain of type II poliovirus which must be considered the etiological agent in this case.

By the t character the isolate is close to wild street viruses (it has the capacity of multiplication at 40°C in tissue culture)/ The presence of similar antibody titers (1:256) to type II virus 23 and 35 days after the onset is not at variance with the etiologic role of type II virus as the maximum immunologic response could develop already by the 23-rd day of illness.

Two months interval between vaccine feeding and onset of the disease indicates against the association of the disease with vaccine feedings.

Case 5. - Toevjalja, M.E., a girl of 10 years (Rakvere). Received two feedings of trivalent live vaccine (on April 23 and May 21).

She felt ill on July 27 (two months after a second feeding), with fatigue and weakness in the legs, followed by pains on July 28. Two days later she could not walk without support; sat leaning upon the hands. There was no fever. The patient was hospitalized, 8 days after the onset. Neurological examination upon admission revealed mild opisthotonus, tenderness of sciatic nerves and paravertebral nerve points in the lumbo-thoracic part, hypotonic muscles of the extremities, reduced

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force of grasp in the hands and reduced shoulder abduction, no movement in the feet, absence of tendon and periosteal reflexes and abdominal reflexes. Nine days after the onset the cerebrospinal fluid contained 3 cells per cmm, protein 0.8°/oo.

The treatment resulted in recovery of muscle function, more rapid in proximal parts and slower in distal ones.

Twenty days after the onset muscle atrophy appeared in m.m. supra- and infra-spinatus. At discharge 40 days after the onset muscle atrophy of the shoulder girdle and thorax, atrophy of shin muscles, more marked on the left side, mild kyphosis of thoracic and increased lordosis of lumbar spine were observed.

Such a detailed description of clinical symptoms and signs is given because 11 days after the onset a nonpoliomyelitis cytopathogenic virus was isolated from stools. It could be identified neither as any one of the poliovirus types, nor as their mixture, but was neutralized by a mixture of specific immune sera to ECHO viruses (types 5, 6, 7, 8). The isolation of this virus does not rule out poliomyelitis nature of this disease, but in a similar case Roca-Garcia et al (5) isolating Coxsackie A-4 virus from stools of a paralytic patient, associated the etiology of paralytic disease with the isolated euterovirus. This is based on recently accumulating data indicating that some euteroviruses may sometimes cause diseases with paresis and paralysis. Such possibility is likely to exist in our case. Serologic data are not contrary to this assumption because at 11 and 72 days antibody titers to all three poliovirus types remained unchanged, therefore it is difficult

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to associate this disease with poliovirus.

Case 6. - Vasilyev, V.L., a boy of 12 years (Lihula district). Vaccinated on March 31 with type I, May 8 with type III and June 8 with type II live poliovirus vaccine.

The boy felt ill on August 15 with fever and headaches followed by weakness in the legs on the next day and in the arms on the third day. At 6 days dysarthria and dysfunction of the tongue movement were noted, and two days later bilateral paralysis of mimic musculature of the face, weakness of masseteric muscles and of the tongue developed. 7 days after the onset increased protein value and cytosis of 3 cells per cmm were found in the cerebrospinal fluid. Hospital treatment resulted in complete recovery of function of mimic, masseteric and deglutitive musculature, The patient began to walk unsupported, impaired reflexes recovered, but the weakness of dorsal flexion of the feet persisted.

Stool specimen collected 14 days after the onset yielded a virus which could not be typed by poliomyelitis immune sera. Unlike the previous case, however, wild type I poliovirus may be suggested as the etiologic agent despite the isolation of nonpoliomyelitis virus, as during the period from 6 to 16 days after the onset, antibodies to type I poliovirus developed and reached the titer of 1:16. Previous vaccination with type I virus (on March 31) did not produce any immunologic response in the patient. Accordingly, development of type I antibody indicates a recent infection with this type and no association with the live virus vaccination.

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Case 7. - Eigi, K.A., a man of 29 years of age (Poltsamaa district). Received one feeding of type I live vaccine on April 10.

He fell ill on August 24 with pains in the back and heavy head. With these symptoms he continued to work till August 29. On this day fever (38°C) developed. On August 30, the patient could not walk because of severe weakness in the legs which progressed to complete paralysis two days later. The temperature was high (38°C). The patient was hospitalized and remained in the hospital till November 6.

Neurological examination on September 2 revealed slight rigidity of occipital muscles and paralysis of the lower extremities. Minimal abduction of the left thigh and slight dorsal flexion of the left foot were present. Abdominal reflexes and those in the legs were absent. Later in the course the condition slowly improved. In 3 to 4 weeks muscles became hypotonic and atrophic.

Negative results of virologic tests with stool specimens and the fact that the first blood specimen was obtained late in the disease (18 days after the onset) make the interpretation of etiology of this case difficult. Type II poliovirus may be assumed to be the etiological agent, because the titer of antibodies to this type increased 2-fold during convalescence. This case was definitely not associated with live virus vaccinations.

Case 8. - Jalajas, U.P., a girl of 15 years of age (town Torva). Received two feedings of the live vaccine: type I (April 8) and type III (May 8).

The girl became ill on September 16 with muscle pain in

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the legs. On September 21 myalgia was diagnosed and bed rest prescribed. There were no other symptoms and no fever. Eight days later a neurologist diagnosed poliomyelitis with weakness in the left leg. The patient was hospitalized. At 20 days after the onset there was no weakness in the legs, but Achilles reflex was absent on the left side.

Stool specimen collected at 29 days yielded type I poliovirus which must be the causative agent in this case. The long interval between the date of feeding with type I virus and the onset of the disease indicates no association of this disease with vaccinations.

Case 9. - Polikashova, T.N., a girl of 4 years (town Kohtla-Jarve). Received two feedings with trivalent mixture of the live vaccine on April 10 and May 28.

The girl became ill on September 20. The parents noticed that her mouth was twisted and one eye did not close. There was no other symptoms. Examination on admission (September 23) revealed facial palsy, anisoreflexion of patellar reflexes (D < S) and deviation of the tongue to the right. The cerebrospinal fluid was not tested. At 15 day the girl could close the eye almost completely. At 31 days there was a slight difference between nasolabial folds, and at 35 days after the onset the child completely recovered.

No laboratory investigation was done in this case. The long interval between vaccine feedings and the disease (about 4 months) indicates no association with vaccinations in this case too.

Conclusions

1. In all investigated cases of poliomyelitis in

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vaccinated persons with the live vaccine there was either no antibody against the etiologic type of the virus or the level of antibody was negligible. Thus the possibility of paralytic poliomyelitis development in the vaccinated is related to the fact that after the complete cycle of vaccinations some persons do not acquire immunity to one or more types of poliovirus.

2. The fact that after mass vaccination program 7 out of 8 poliomyelitis cases reported in June-September, 1959 were in the vaccinated is explained by high proportion of the vaccinated in Estonia (58.1 per cent of the total population). Since in come cases ingestion of the vaccine does not provide the necessary immunity for a number of reasons (interference between viruses in the intestinal tract and others), with the increase in number of the vaccinated the number of persons left susceptible to poliovirus after immunization is increasing.

3. Even with large-scale immunization of the population street strains of poliovirus still find some conditions for preservation and limited circulation among the population.

4. For compensation of some cases of vaccination failure and for creation of higher immune strata among the population it is advisable to carry out revaccination with the live poliovirus vaccine periodically.

5. In investigation of paralytic poliomyelitis cases among the vaccinated with the live vaccine possible etiological role of some nonpoliomyelitis enteric viruses should be taken into consideration.

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References

1. Chumakov, M.P. - "On mass oral immunization of population in the Soviet Union against poliomyelitis with live vaccine from A.B.Sabin's attenuated strains", Moscow, 1960.

2. Chumakov, M.P., Voroshilova, M.K., Vasiljeva, K.A., Bakina M.N., Dobrova, I.N., Drozdov, S.G., Podsedlovsky,T.S., Kostina, K.A., Shirman, G.A., Yankevitch, O.D., Uspensky, J.S., Ashmarina, E.E. - Problems of Virology, 1959, 5, 520/

3. Benyesh-Melnick, M., Melnick, J.L. - Live poliovirus vaccines, USA, Washington, 1959, p. 179.

4. Drozdov, S.G., Shirman, G.A. - Interference between street and vaccine poliovirus strains in the human intestinal tract. - Presented at Virology Section of Moscow Department All-Union Society of microbiologists, epidemiologists and infectionists, February 17, 1960.

5. Roca-Garcia M., Orsi, E., Markham, F., Bacigalupi, J., Doany, H., Tossi, H., Cabasso, V., Moyer, A., Cox, H. - Live poliovirus vaccines, USA, Washington, 1959, p. 648.

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Table 1

Results of investigation of poliomyelitis cases in the vaccinated in Estonian SSR, April-September, 1959

Case No.:	1	2	3	4	5	6	7	8	9
Name	Mardim, V.E.	Reigo, M.K.	Kutjev, V.A.	Marja, K.V.	Toevjalju, M...	Vasiljev, V.L.	Eigi, K.A.	Yalajas, U.P.	Polikashova, T.N.
Place of residence	district Harju	Tallinn	district Atja	Tallinn	Pakvere	District Lihula	district Polt-sama	Torva	Kohtla-Yarve
Age	5 years	17 years	2,5 years	16 years	10 years	12 years	29 years	15 years	4 years
Date of outset	2/IV	26/V	20/VI	6/VII	27/VII	15/VIII	24/VIII	16/IX	20/IX
Dates of vaccine feeding	1st type I 11/III	type I 18/III	type I 8/IV	type I 17/III	I+II+III 29/IV	type I 31/III	type I 10/IV	type I 8/IV	I+II+III 10/IV
	2nd not given	I+III 16/IV	type III 15/V	I+II 16/IV	I+II+III 21/V	type III 8/V	not given	type III 8/V	I+II+III 28/V
	3rd not given	I+II+III 23/V	type II 10/VI	I+II+III 7/V		type II 8/VI	not given	not given	
Results of tests with stool specimens	1st 10/IV -	1/VI -	8/VII -	29/VII -	7/VIII +	26/VIII	napo 26/IX -	15/X + (type I)	not tested
	2nd 14/IV -	4/VI -		4/VIII +	(virus	29/VIII+	lio 15/X -		
	3rd 20/IV + (type II)	8/VI + (type I)		type II)	from ECHO	1/IX	vime		
	4th	19/VI -		8/VIII -	group)				
Date of 1st blood specimen collection	10/IV		1/VII	29/VII	7/VIII	21/VIII	11/IX	not tested	not tested
2nd	26/V	19/VI	8/VII	10/VIII	7/X	31/VIII	26/IX		
Results of tests for antibody x) in sera	type I 1:4		1:4	1:4	1:128	1:4 xx)	1:128		
	type II 1:4		1:128	1:256	1:512		1:8		
	type III 1:4		1:8	1:8	1:4		1:16		
2nd	type I 1:4	1:8	1:4	1:4	1:128		1:128		
	II 1:4	1:512	1:512	1:256	1:512		1:16		
	III 1:4	1:4	1:16	1:16	1:8		1:16		
Rate of antibody increase	type I no		no	no	no	4x	no		
	type II no		4x	no	no		2x		
	type III no		2x	2x	no		no		
Probable type of the causative agent	type II	type II	type III	type II	Virus from ECHO group	type II	type II	type I	?

x) Sera tested in the complement-fixation test (Chumakova, M.J.)
xx) Sera tested in the neutralization test is tissue cultures of human fibroblasts

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Table 2 - Results of tests by t character of polio-virus strains isolated frmm stools of polio-myelitis patients (Estonian SSR, 1959).

Case No.	Patient	Virus type	Log_{10} TCD_{50}/ml at 36°C	Log_{10} TCD_{50}/ml at 40°C	EOG
1	Mardim	II	7.2	6.2	1.0
2	Reigo	I	6.1	0.0	6.1
3	Märja	II	6.0	3.7	2.3

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ACADEMY OF MEDICAL SCIENCES OF THE USSR

INSTITUTE FOR POLIOMYELITIS RESEARCH

STAT

Immunization with live poliovirus vaccine and preliminary data on its effectiveness

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Poliomyelitis incidence in western regions of the Ukraine increased gradually in the pastwar years. Since 1956 separate outbreaks of this infection began to be reported. Current control and sanitary measures did not bring any reduction of the incidence.

In 1958 planned vaccination programs with killed vaccine injections were started. Despite much effort and work of the sanitary-epidemic service the coverage with vaccinations was not great, hence no marked reduction of poliomyelitis incidence was observed.

In July 1959 under direction of Lvov Institute of Epidemiology, Microbiology and Hygiene vaccination of children with trivalent live poliovirus vaccine from A.B. Sabin's strains was carried out in Chervovtsy, Stanislav and Ternopol regions; in December, 1959, children were immunized with the live vaccine in dragée-candy in Volynsk and Rovno regions, and a month later in Poltava and Lvov regions.

Organization of vaccinations

The vaccine was manufactured at the Institute for Poliomyelitis Research, Academy of Medical Sciences of the USSR (Moscow) and was shipped by air. At first it was stored at sub-zero refrigerators at the Institute, later cold chambers of local food industry enterprises were used for storage of the vaccine in the regions.

From these cold chambers the vaccine was transported to the laboratory for dulition and then to vaccination centers in large thermos flasks on ice mixed with salt, in which, with good packing, a temperature below zero lasted for over 24 hours.

The vaccine was diluted with Hanks' salt solution, the procedure being performed by an experienced virologist at premises

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of regional sanitary-epidemiological station. The diluted vaccine was distributed into penicillin vials in 100-150 and 200 doses, and was transported to local vaccination clinics in thermos flasks on ice. The program was planned so that diluted vaccine was used on the day it was prepared.

All these measures provided optimal conditions for vaccine virus survival which was considered one of the main factors for development of good immunity in the vaccinated.

One center for vaccine dilution could supply the vaccine for mass immunization of children in 2 or 3 areas in one day.

For successful carrying out of the program on the appointed day all medical personnel of the area was mobilized, only workers on duty being left in polyclinics and hospitals. Great help was provided by local communist party and Soviet offices.

The simplicity of the procedure of immunization with the live vaccine and good spade work made it possible to carry out vaccinations in the shortest time. For example, in Chernovtsy region, immunization of children aged 2 months to 17 years with liquid trivalent live vaccine was carried out in 15 days. The use of dragée-candy leads to further shortening of periods necessary for vaccination. Thus, in Rovno, Volynsk and Poltava regions children of similar ages were immunized with dragée - vaccine in 3 to 4 days.

Organized children were vaccinated in nurseries, kindergartens, schools, unorganized children and also schoolchildren during summer vacations received the vaccine in vaccination clinics.

To avoid overcrowding of children in premises of vaccination clinics in winter time medical personnel visited unorga-

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nized children at home and gave them the vaccine there.

Our practice indicates that in regions where immunization was carried out in the shortest time the coverage with vaccinations was more complete. Great spade-work is necessary for organized carrying out of immunization.

Table 1

Number of children vaccinated with trivalent live poliovirus vaccine x)

Regions	Total population	Vaccinated			Revaccinated		
		Trivalent	No.	%	Trivalent vaccine	No.	%
Chernovtsy	707,000	liquid	256,237	36.2	Dragée	204,259	28.9
Stanislav	1,100,100	liquid	272,856	23.0	Dragée	204,950	18.6
Ternopol	1,090,000	liquid	255,112	23.4	Dragée	243,008	22.3
Volynsk	890,000	Dragée	269,317	30.3	Dragée	262,058	29.4
Rovno	921,000	Dragée	270,000	29.3	Dragée	252,817	27.4
						1,167,092	88.1

Exact data of the numbers of children in these regions were not available, therefore Table 1 presents numbers of total

x) Numbers of population for regions are based on the data published by Information-Statistical Department of the Presidium of the USSR Supreme Soviet in the book "The USSR. Administrative-territorial division of union republics, Moscow, 1958".

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population in the regions. Since vaccination was carried out mainly among children (Table 3), it may be said that in the above regions absolute majority of the population most susceptible to poliomyelitis has been vaccinated. 2-5 months after the first feeding 88 per cent of the vaccinees were revaccinated.

In two regions immunization was performed with monovaccine (Table 2).

Table 2

Number of vaccinated with monovalent live poliovirus vaccine

Regions	Total population	Monovalent vaccine	Vaccinated with Type I		Vaccinated with Type III	
			No.	%	No.	%
Poltava	1,634,000	Dragée	403,919	24.0	-	
Lvov	2,089,000	Dragée	560,000	26.8	520,000	24.9
Total			1,163,919			

Immunization in these regions has not been completed, but the above data show that 1,163,919 persons received type I vaccine and 520,000 persons received type III.

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Table 3

Age-distribution of the vaccinated

Region	Age-groups					Total in the region
	Under 1	1-5	5-10	10-17	17 +	
Chernovtsy	12,899 1.8%	54,269 7.7%	67,697 9.6%	47,486 6.7%	21,908 3.1%	204,259
Stanislav	15,801	58,513	64,149	50,222	20,265	208,950
Ternopol	23,658	86,155	50,661	82,534	16,548	259,556
Volynsk	16,298	64,110	65,389	72,386	3,582	221,765
Rovno	18,259	84, 896	82,197	96,089	1,376	282,817
Poltava	16,397	93,494	124,372	145,260	24,441	403,919
Total	103,312	441,437	454,720	493,977	88,120	1,581,266

Safety and reactogenicity of the live vaccine

Investigation of the live vaccine from A.B. Sabin's strains by scientific workers under M.P. Chumakov's and A.A. Smorodintsev's guidance demonstrated complete safety of the vaccine. On the basis of these data the Ministry of Health of the USSR allowed to use it for large-scale immunization.

In carrying out immunization in the regions we established surveillance of the vaccinated in order to study response of the human body to the vaccine virus ingested and possible postvacci-

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nation complications and to elucidate the nature of diseases reported.

For study of vaccine reactogenicity soon after vaccination we interviewed medical workers, teachers and the vaccinated themselves. For study of possible remote complications pediatricians and neurologists regularly examined 307 children in Poltava and Lvov infants' homes.

In both institutions general status of children surveyed was good both before and after immunization. No objective changes or even slight signs of the central nervous system involvement was observed. Regular thermometry both prior and subsequent to vaccination demonstrated that in all vaccinated children the temperature remained in normal limits.

In Lvov infants' home there were no cases of enteric dysfunction among the vaccinated, in Poltava infants' home of 47 vaccinated children in 4 with stable stools mild transitory loosening was observed.

Thus, observations on infants who are most susceptible to poliomyelitis have revealed complete safety and areactogenity of the live vaccine.

Because in infants only objective signs of disease could be detected we decided on interrogating broadly the vaccinated children of older ages - in kindergartens and schools. As a rule,

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absolute majority of them gave no complaints. Occasionally some schoolchildren and especially vaccinated medical workers, when questioned, complained of dizziness, nausea, enteric dysfunction, drowsiness. On careful examination, however, these complaints could not always be accounted for by vaccine ingestion.

More frequent complaints among medical workers may be explained, in our opinion, by better recognition of any signs of disorder. But the possibility cannot be excluded that these complaints were, to a considerable extent, of psychogenic character.

The live vaccine is a new preparation, and medical workers introducing it on a large scale were alert and the vaccinated were, so to say, expecting complications, looking for them.

For confirmation of this assumption some data may be presented throwing some light on the so-called "reactogenicity" of this preparation.

In the town of Rovno workers of regional sanitary-epidemiological station were immunized one day before the beginning of vaccination program in the region. One man had a convulsive epileptic attack two hours after vaccine ingestion. A physician called to this patient erroneously associated this fit with vaccine ingestion. Since active preparation was in progress to begin vaccination on the following morning the news of this event spread rapidly among medical workers and made them feel on the alert.

After the end of vaccination program about two thousand vaccinated schoolchildren were examined, of them 1 to 2 per cent complained of transitory nausea, mild headaches, entric dysfunction of short duration. At the same time vaccinated medical

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workers told of very variable symptoms, such as dizziness, diarrhea, rhimitis, headache, cough, drowsiness, fever of 38°-39°, sweating, pains in joints, pains in the side. This diversity of complaints shows that they are not associated with vaccine ingestion. Great alertness of the medical workers led to discovery of such symptoms which usually pass unnoticed.

In other regions where there had been no such coincidence, complaints among medical workers were infrequent.

The observations which were carried out suggest that even if the vaccine has any side-effect it is so slightly manifested that the population does not pay any attention. There were occasions of simultaneous ingestion of 50 doses and more, and there were no complications whatsoever.

Effectiveness of immunization with trivalent live poliovirus vaccine

Climatic conditions and cultural and economic levels of all the western regions of the Ukraine are similar. Poliomyelitis was reported predominantly among children population.

Fig. 1 shows that dynamics of poliomyelitis incidence was similar in both groups of regions, that is, it was gradually increasing. In July 1959 large-scale immunization of population up to 17 years of age with live poliovirus vaccine was started in Chernovtsy, Stanislav and Ternopol regions. Fig. 2 shows dynamics of 1959 poliomyelitis incidence in regions where there was and there was no vaccination done.

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Curves in Fig. 2 show that in the first six-month period poliomyelitis incidence in both groups of regions was almost similar. In summer months polio cases became more frequent.

Since Huly in regions where vaccination was started gradual reduction of incidence was noted, since September the reduction was sharp. Here it must be said that in Stanislav and Ternopol regions immunization was gradual, involving about 50-60 thousand children monthly. Therefore reduction in incidence was parallel to decrease in number of unvaccinated. Poliomyelitis cases were reported mainly among unvaccinated. In those regions where absolute majority of children population was involved by vaccinations poliomyelitis in these age-groups was not reported. For example, in Chernovtsy region where 36.2 per cent of the total was immunized there was no poliomyelitis in children during seven months. There was only one case in an unvaccinated adult.

Up to January, 1960, inclusive, among 652 thousand vaccinated in three regions, three cases of disease were reported, two of them with transitory facial palsy. These cases were diagnosed as poliomyelitis by clinicians. Laboratory studies were not done. Even if this diagnosis is accepted, then among the vaccinated the incidence was 0.46 per 100,000, whereas among the unvaccinated in the same period the incidence was 10 per 100,000, that's many times higher.

Occurrence of poliomyelitis cases among the unvaccinated and almost complete absence of cases among the vaccinated confirm once more high prophylactic value of the live vaccine. These data indicate that during the above-mentioned period

1960

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some circulation of wild (street) poliovirus was still in progress but because of lack of sufficient susceptible population it did not cause any spread of poliomyelitis incidence.

Conclusions

I. Observations on the vaccinated in some regions of the Ukraine have confirmed complete safety of the live vaccine from Sabin's strains manufactured in Moscow. There were no complications after feedings. Untoward reactions to the ingested vaccine, observed in some cases were so mild that the population did not pay any attention to them.

2. Only isolated cases of poliomyelitis were observed among those receiving one feeding of the vaccine. The cases had a very mild course without any residual signs.

3. Observations carried out in 1959 in the Ukraine confirm high prophylactic value of the live poliovirus vaccine. In the second six-month period of 1959 poliomyelitis incidence among the vaccinated was approximately 20 times lower than that among the unvaccinated.

4. Simplicity of the immunization procedure allows to carry out mass vaccination of the population in short time which is very important for poliomyelitis control.

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ACADEMY OF MEDICAL SCIENCES OF THE USSR

INSTITUTE FOR POLIOMYELITIS RESEARCH

STAT

THE EXPERIENCE OF MASS EMPLOYMENT OF LIVE POLIOVIRUS VACCINE DURING THE MORBIDITY INCREASE IN THE TASHKENT CITY

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In the Uzbek SSR poliomyelitis in the form of sporadic cases and inconsiderable outbreaks is registered for a period of more than 30 years.

The period from 1926 to 1939 is characterized by an annual registration of up to 50-85 cases of poliomyelitis throughout the republic with a population of 7-8 million. During this period there were two comparatively moderate outbreaks of the disease: 239 cases in 1929 and 297 in 1938. From 1940 to 1949 there was an annual registration of 1-6 cases of poliomyelitis in the whole republic; in 1944 and 1947 not a single case of poliomyelitis was observed.

Finally, from 1950 to 1958 there was noted a gradual growth of the incidence of poliomyelitis, which ended with the largest outbreak in 1959. Urban inhabitants comprised the major proportion of all the patients. Table 1 depicts the dynamics of poliomyelitis during this period in the Uzbek SSR.

The correlation between the urban and rural poliomyelitis incidence from 1950 to 1958 is shown in figure 1. The incidence rate of the morbidity was 4-5 times higher in towns than in rural districts. The incidence of poliomyelitis was preponderant in the Tashkent City, the Tashkent, Fergana and Samarkand Regions. The incidence rate of poliomyelitis according to regions of the Uzbek SSR in 1958 and 1959 is given in table 2.

An analysis of the seasonal prevalence of poliomyelitis for 1950-1958 according to an average monthly number of cases shows that a rise in the morbidity usually occurs in

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June, reaching its maximum in July. In August and September the morbidity is still high, starting to decline in October. In the course of June-October there is registered on the average 57.5% of the annual number of cases (table 1).

Table 2

INCIDENCE RATE OF POLIOMYELITIS ACCORDING TO REGIONS OF THE UZBEK SSR IN 1958 and 1959 (PER 100,000 POPULATION)

Region / Year	Tashkent	Andizhan	Bukharskaya	Kashkadaryinskaya	Namangapskaya	Samarkandskaya	Surkhandaryinskaya	Fergana	Khoresm	Karakalpakskaya ASSR
1958	3	2	4	0.2	1	4	0	5	1	0.2
1959	18	5	4	2	3	4	3	8	8	0.9

The average figures do not reflect the fluctuations in the seasonal prevalence of poliomyelitis in different years. The largest upsurge of the morbidity in 1952 and 1957 was noted in July; in 1956 - August, in 1953 - September, in 1951, 1954 and 1955 - November.

According to data of the last years the largest incidence of poliomyelitis occurred in the age group of from 0 to 4 years (87.9%), in this group the morbidity was prevalent in children, aged from 6 months to 2 years (59.7%).

During the last years the morbidity in Tashkent showed a tendency towards a gradual increase (figure 1, table 3) and comprised annually from 25.1 to 79.2% of the entire poliomyelitis incidence in the Uzbek SSR.

During the 5 years (1954-1958) preceding the 1959 poliomyelitis outbreak there was seen a definite tendency towards a relatively slow growth of the incidence (1954 -

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29 patients, 1955 - 34 patients, 1956- - 49 patients, 1957 - 66 and 1958 - 96 patients).

The incidence rate per 100,000 population in Tashkent during 1956-1958 amounted to 5.3-10.5, while that per 100,000 children aged up to 14 years (inclusive) - 28.0 (1957) and 37.0 (1958) (See table 4).

Such was the general picture of the incidence of poliomyelitis in the Uzbek SSR and Tashkent prior to 1959.

The annual increase of the number of affections (figure 1) was a serious warning of the possibility of an epidemic outbreak of poliomyelitis. In connection with this, in 1958 preventive inoculation with killed vaccine were started in the Uzbek SSR. In the republic single vaccination was effected in 9,800 persons, of whom 9,370 in the city of Tashkent.

The first 5 months of 1959 proved favorable in respect to poliomyelitis incidence. For this period 35 cases were recorded in the republic, while in 1958 during these months there were already 93 cases, the average number for 9 years being 36. In Tashkent from January to May 9 persons fell ill. For the same period in 1958 there were recorded 27 patients, the average number for 5 months during 1950-1958 amounted to 12.8.

In June a sharp change took place. During this month in Tashkent 37 persons contracted the disease, of them 27 in the second half of the month. In the other cities and regions of the republic a rise of the poliomyelitis incidence started in July.

In connection with the increase of the morbidity in the Uzbek SSR vigorous antiepidemic measures were elaborated.

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In particular, in accordance with the advice as well as the participation of Professor M.P.Chumakov, a decision was reached to institute in short terms, first in Tashkent and then in the whole republic, an all=round peroral immunization of all children up to 15 years old with live poliovirus vaccine from A.B.Sabin's strains, prepared in the Institute for the Study of Poliomyelitis of the AMS of the USSR. By this time the live poliovirus vaccine from Sabin's strains has already passed mass trials in the Estonian and Lithuanian SSR, Moscow Region (1.2) and other places of the Soviet Union.

The possibility of successful employment of live vaccine during an epidemic outbreak of poliomyelitis was mentioned in the works of Curtua, Koprovsky, Lebruen and others in 1959; Plotkin and others in 1959 according to immunization data in 1957 in the Belgian Congo. In accordance with A.B.Sabin's recommendation Hale with collaborators used for the first time in 1958 a live vaccine from Sabin's type 2 strain for the epidemic control in Singapore, caused by the type I. The live vaccine produced a favorable effect. It was explained by the phenomenon of interference of the type 2 vaccine virus with street strains. However, in Hale's experiment the vaccine was employed during the decline of the epidemic curve, i.e. relatively late.

During the virological examination of patients with poliomyelitis in Tashkent (June-July, 1959; according to data of S.S.Maksumov) the majority of isolated strains proved to be type I poliovirus (73.5% - type I, 14.9% - type 2, 5.2% - type 3). Consequently, this type, as in

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many other large outbreaks, was the principal etiological causative agent of the disease.

In order to more fully utilize not only the specific immunization with the vaccine virus, but also the interference phenomenon of the live vaccine between the street poliomyelitis strains, it was decided to use in the Uzbek SSR a trivalent mixture containing a vaccine against 3 immunological types.

The main complex of measures for the poliomyelitis control in Tashkent and throughout the Uzbek SSR consisted of the following sections:

1. Prompt detection and immediate hospitalization of patients and suspects with subsequent disinfection in the focus and in the surroundings.

2. Observation over subjects having had contact with poliomyelitis patients and hospitalization of the former when necessary.

3. Single=stage, i.e. conducted in short terms, mass immunization of all children, aged from 2 months to 15 years with live poliovirus trivalent liquid vaccine.

4. Improvement of the sanitary condition of the inhabited areas.

5. Mass=scale sanitary education work among the population.

All the measures referred to above were organized by the antipoliomyelitis center and the Sanitary Epidemiologic Service of the Ministry of Public Health of the Uzbek SSR, under the management of the Deputy Minister of the Public Health of the Uzbek SSR - K.S.Zairov.

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Great help in the institution of measures for poliomyelitis control was rendered by the Central Committee of the Communist Partee and the Council of Ministers of the Uzbek SSR, the Tashkent City Committeeof the Communist Partee of the Uzbek SSR, as well as by local Party and Soviet organizations. Particular attention was paid to the conduction of the vaccination.

Undiluted monovaccines (type I, II and III) were delivered to Tashkent via the air service in a frozen state on dry ice in batches containing 200,000-500,000 doses. Prior to utilization the preparation was stored in a low=temperature refrigirator of the Tashkent Institute of Vaccines and Sera (SRIVS). In this Institute there was performed the mixing of the three types of vaccines, their dilution (1:10) and bottling into insulin bottles (3-5 ml, or 30-50 doses). Before use the diluted vaccine was preserved at $+2^0$—$+4^0$C (as a rule, not more than 1-2 days).

The delivery of the vaccine to medical institutions of Tashkent and near=lying towns and regions was effected by transport facilities. To remote districts the vaccine was sent via the air service, with accompanying medical personnel. During transportation the vaccine was continuously cooled with melting ice.

Before the vaccination there were held instructive meetings and seminars for medical workers on problems pertaining to the use of live poliovirus vaccine.

The major part of the inoculations was effected by the house=to=house method. Special inoculation centers, which organized and instituted the vaccination in their respective districts, were created in the towns and inhabited areas on the basis of medical instututions (mainly in polyclinics and

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children's health centers). The territory of the district was divided into sections. A special inoculation team was assigned to each section (usually a physician and two nurses). During the inoculations the medical workers follow the directions of the "Instruction for the Vaccinator", elaborated by Prof. M.P.Chumakov and printed typographically.

All children, aged from 2 months to 15 years inclusive, were vaccinated without consideration of any contraindications (this also includes feverish and noninfectious patients undergoing treatment in hospitals). Registration of the inoculated was carried out according to a special list. Polyclinics and children's health centers supervised over the course of vaccination, its proper management and had under control the registration and the population coverage rate.

The vaccination in Tashkent commenced on July 19th. During this day over 2 thousand medical workers of the city took part in the vaccination. As the result of this 182,000 children were inoculated during that day and 131,427 more during on the 23rd-24th of July. Thus, during three days 313,427 children up to 15 years of age were vaccinated in Tashkent, in the following two weeks nearly 7,000 children. The total number of vaccinated was approximately 320,000, comprising nearly 94% of the above age group.

At the railway station, airport and bus terminals there were organized vaccination posts, where all children arriving into the city were subject to inoculation.

In Tashkent during September repeated vaccination with trivalent live vaccine was conducted, embracing 313,100 persons.

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The experience gained in Tashkent was popularized in other towns and regions of the republic. As a rule, in other areas the vaccination was effected promptly, in a course of several days. During the period from July to September in the Uzbek SSR 2,409,000 persons underwent single vaccination, i.e. about 30% of the population.

Widespread information of the population played a paramount role in the institution of the vaccination and other measures for the poliomyelitis control. The sanitary education services employed various measures for this purpose. There was organized a series of lectures and discussions in which participated professors and general practitioners. These lectures and discussions were broadcasted through the radio and television network. The radio was also used for informing the population of the terms and places where the inoculation is done. Articles on poliomyelitis were published in the republican and regional newspapers in the Russian and Uzbek languages. There was also published a special popular brochure and several leaflets on this subject, with a circulation of 300,000 copies (in Russian and Uzbek languages). As the result of wide sanitary eduction work in connection with poliomyelitis control various sections of the population were enlisted.

The principal remedy in the general complex of measures for poliomyelitis control was the live trivalent vaccine. Analysis of the results of its employment during the epidemic outbreak in Tashkent is of paramount importance for the practice of mass vaccination.

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On figure 2 is shown the weekly incidence of poliomyelitis in Tashkent, whereas on figure 3 - the daily incidence during July=September. A sharp rise of the morbidity started in the second half of June (from the 26th week). For a course of three weeks the morbidity continued to increase. Vaccination was effected on the 4th week of the outbreak; 6 weeks following the vaccination the incidence dropped down to the usual nonepidemic level. The whole period of the outbreak comprised 9-10 weeks.

A rapid increase of the poliomyelitis incidence in a large populated area during the first half of the summer is usually indicative of a prolonged and massive epidemic.

If we shall consider the seasonal course of poliomyelitis incidence in the Kazakh SSR, closely associated with the Uzbek SSR by many conditions, it would be seen that massive outbreaks, for instance in Alma=Ata and Alma=Ata Region, involve a period of 4½-5 months, or 18-20 weeks (figure 4).

The 1958 epidemic in Singapore described by Hale (1959) lasted for over 16 weeks (figure 5); during the second half of the outbreak nearly 50% of the infantile population of Singapore was vaccinated with live poliovirus vaccine. Hale is of the opinion that this measure was conducive to the shortening of the period of the epidemic and reduced the number of affected children.

The Tashkent outbreak, notwithstanding an unfavorable prognosis regarding the extent and period, was under control considerably sooner than analogous epidemics in large cities, where conditions are propotent for a protracted course of the epidemic. The rapid and continuous drop of the morbidity in Tashkent following mass vaccination is a direct sequence of this immunization with live poliovirus vaccine.

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For proper assessment of the role of vaccination in the initial rapid decrease of the poliomyelitis incidence it is deemed necessary to consider the possibility of nonspecific interference of the vaccine, cutting short the "chain" of street virus transmission at the expense of the more rapid distribution of the vaccine virus by way of vaccination of the whole population. The essence of nonspecific protection of this kind lies in that the street virus could not adjust itself and propagate in the intestine of subjects in whom a vaccine virus is propagating (the interference phenomenon). Laboratory investigations, conducted on materials of the Estonian SSR (Drozdov, S.G., Shirman, G.A., 1960) demonstrated that the vaccine virus entering the intestine in a large dose could even oust in a number of instances the street virus already inhabiting the intestine, which could intensify the early nonspecific effectiveness of the vaccination.

On the 3rd-4th week following vaccination the specific immunity, as a rule, acquires its importance, increasing the resistance of the inoculated persons to the street poliovirus.

It should be considered, however, that during the period of high poliomyelitis incidence infection of the population with the street virus assumes enormous proportions. As the result of this in a number of the inoculated - carriers of the street virus - the vaccine virus could be supplemented with the street virus. However, during mass and single-stage vaccination an enormous proportion of the carriers of the vaccine virus, apparently, creates the necessary prerequisites for a rapid arrest of street virus

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circulation. On figure 6 an attempt was made to present graphically the interaction of two counter=processes - distribution of the vaccine virus with the development of nonsusceptibility to street virus infection, with the subsequent development of poliomyelitis or latent immunization.

The contingents of subjects inoculated could be divided into three groups: 1) persons free at the time of vaccination from intestinal viruses carrier state and completely nonsusceptible to the inoculation; 2) carriers of the epidemic poliovirus and 3) carriers of other intestinal viruses. The two latter groups may temporarily be practically refractory to peroral inoculation.

The inoculation could be effective for all persons of the first group, as well as for those of the second and third groups, in whom the process of intestinal carrier state was either not yet established, or was coming to an end and the street virus or enterovirus of other etiology could be ousted by the vaccine virus.

The other part of the 2nd and 3rd groups, for whom the vaccination was ineffective, represent a scene of further rivalry of viruses. A number of persons of the 2nd group infected with the street virus contracted the disease, inasmuch as they were in the incubation stage at the time of vaccination. Another proportion, becoming freed from the street virus of poliomyelitis without pathological symptoms, could be vaccinated via the contact route with those types of vaccine virus to which the organism had no immunity. Persons of the third group, as soon as they were liberated from the enteroviruses, became the victim of either the

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street virus, the circulation of which was already sharply reduced, or accepted the vaccine virus from those inoculated by the contact route and became immune.

Inasmuch as the vaccination, naturally, should have sharply reduced the circulation of intestinal viruses and has prevented further transmission of enterovirus infection, one could suppose that the majority of persons of the third group, who were not susceptible to the vaccine virus during the vaccination, were a sufficiently homogenous group in accordance with the terms of infection with enteroviruses. This, possibly, explains the fact of a certain stability of the morbidity on a relatively low level on the 33rd-34th week. Possibly towards this period a considerable group of entero-viruses carriers became susceptible to the poliomyelitis virus. Some of them recieved the vaccine virus by way of contact, the other became infected with the street virus and gave an additional number of cases of paralytic polio-myelitis.

The difference in the morbidity among the vaccinated and nonvaccinated in Tashkent (figure 7) speaks in favor of the efficacy of the vaccination. The incidence rate for a six-week period following the vaccination among the non-vaccinated subjects was 3.4 times higher than among the vaccinated ones

A statistical analysis of the χ^2 criterion divulges complete reliability of this difference in the incidence.

The fact that during the last months of 1959 (October, November, December) the number of persons who fell ill in Tashkent was considerably lower the average indices for the past 9 years (see table 1).

The age structure of the affected in Tashkent during the summer season of 1959 and the morbidity in each age

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group are shown in figure 8. The majority of diseased comprised children under 3 years of age (89.3%). In this respect the morbidity in 1959 has the same specific features as that of the preceding years. A schedule of the incidence rate according to age groups depicts that in 1959 the degree of affection of the lower age groups was considerably higher than in the preceding years.

An analysis of clinical observations over the poliomyelitis cases during the summer of 1959 (E.N.Dronskaya, I.S.Sokolova) testifies that among those who had contracted the disease after 21 days following the vaccination there is noted a large percentage of mild forms of the affection in comparison with the nonvaccinated persons.

The territorial distribution of the incidence in the city was irregular. The average incidence rate per 100,000 children under 15 years for the summer period amounted to 118.5. Kalininsky and Karasuisky districts, as well as the Oktyabrsky district of the city displayed the highest incidence. The Kalininsky and Karasuisky districts were previously a/suberb (rural) of Tashkent and only in 1959 they became a former part of the city. Their sanitary condition was on a more inferior level in comparison with the central districts of the city. The Oktyabrsky district is a densely populated part of the old city where there remain badly organized (in the sanitary respect) houses. Thus, during the epidemic outbreak of poliomyelitis in Tashkent in 1959 the most affected were the least favorable, in the sanitary respect, districts of the city.

A number of supplementary conditions (inadequate refuse disposal, extremely limited measures for the prevention of

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poliomyelitis in the preceding years) were also conducive to the development of the outbreak.

A rise in the poliomyelitis incidence was observed in 1959 also in the Tashkent Region (209 cases - an index per 100,000 population of 18.0), Fergana Region (72 cases - an index per 100,000 population of 8.0), however at a later date than in Tashkent (the beginning of the incidence rise in July, the peak - in the beginning of August).

CONCLUSIONS

1. The poliomyelitis incidence in the Uzbek SSR gradually increasing its impetus during the last years has reached in 1959 the level of an epidemic outbreak. The center of the outbreak was Tashkent, where the incidence rate per 100,000 population comprised an annual value of 40.0 (4 times higher than in 1958). The principal number of poliomyelitis cases was associated with the type I virus.

2. Mass vaccination with live trivalent vaccine against poliomyelitis at the end of the 4th week following the onset of the outbreak, involving more than 90% of the Uzbek SSR population under 15 years of age, was conducive to a rapid decline of the incidence and, possibly, to a shortening of the extent and terms of the outbreak. In favor of the effectiveness of the vaccination also speaks the considerably reduced morbidity (according to the incidence rate) among the vaccinated as compared with the nonvaccinated.

3. A speedy approach of the turning point in the course of the poliomyelitis outbreak in Tashkent following mass employment of live vaccine could not be explained only by the development of the immunity. Of major importance was

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the interference between vaccine and street poliovirus, as the result of rapid dissemination of the vaccine virus due to vaccination and mechanical disruption of the "chain" of street poliovirus transmission.

4. Vaccination with live trivalent poliovirus vaccine during the summer epidemic outbreak has fully justified itself and could be recommended in the future if a similar situation develops.

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4. Вакцинация живой полиомиелитной тривакциной в условиях летнего эпидемического подъема заболеваемости полностью себя оправдала и может рекомендоваться на будущее при возникновении подходящей ситуации.

ЛИТЕРАТУРА

I. Чумаков М.П. и сотр., Вопр. вирусол., I959, 5, 520.

2. Чумаков М.П. и сотр., О массовой пероральной иммунизации населения в Советском Союзе против полиомиелита живой вакциной из аттенуированных штаммов А.Б.Сэбина, М., I960.

3. Courtois G., Flack A., Jervis G., Koprowski H., Ninane G., Brit. Med. Journ., 1958, July 26, p. 187.

4. Lebrun A., Cerf J., Gelfand H., Courtois G., Koprowski H., in Live poliovirus vaccines, USA, Washington, 1959, p. 410.

5. Plotkin S., Koprowski H., ibid., p. 419.

6. Hale J., Doraisingham M., Lee L., Kanagaratnam K., Leong K., Mon-

7. Дроздов С.Г., Ширман Г.А. Интерференция между уличными и вакцинными штаммами вируса полиомиелита в кишечнике человека. Труды 4-й научной сессии Института по изучению полиомиелита АМН СССР и Международного симпозиума по живой вакцине против полиомиелита. Москва, I7-20 мая I960 г.

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Таблица I.

ЗАБОЛЕВАЕМОСТЬ ПОЛИОМИЕЛИТОМ В УЗБЕКСКОЙ ССР В I950-I958 г.г.

Годы	месяцы												Всего	Годовой % к общему количеству случаев за 9 лет	Показатель заболеваемости на I00.000 населения +)
	I	II	III	IУ	У	УI	УII	УIII	IX	X	XI	XII			
I950	4	3	5	2	5	7=)	5	7=)	2	7=)	3	3	53	4,7	
I95I	5	4	3	I	0	2	2	3	3	2	6=)	3	34	3,0	
I952	4	4	3	2	6	22	25=)	II	8	3	4	2	94	8,4	
I953	2	5	6	9	6	7	6	7	I0=)	4	3	I	66	5,9	
I954	9=)	7	0	5	2	6	7	5	6	6	9=)	8	70	6,2	
I955	4	6	4	3	5	I2	I4	5	9	I3	I9=)	I4	I08	9,6	
I956	9	I0	7	6	I4	23	28	30=)	24	I9	I3	I2	I95	I7,4	2,4
I957	I2	7	I3	I9	I0	20	4I=)	34	25	I5	I5	I7	228	20,4	2,8
I958	I7	I4	I6	I3	33	52=)	36	24	28	2I	I3	6	273	24,4	3,4
Общее количество случаев за 9 лет	66	60	57	60	8I	I5I	I64	I26	II5	90	85	66	I.I2I	I00,0	
%	5,9	5,4	5,I	5,4	7,2	I3,5	I4,6	II,2	I0,2	8,0	7,6	5,9	I00,0		
Среднее количество случаев за I год	7,3	6,7	6,3	6,7	9,0	I6,8	I8,2	I4,0	I2,8	I0,0	9,4	7,3	I24,6		

Примечание: =) Максимальное количество случаев за I месяц в течение соответствующего года.
+) Вычислено на основе данных Всесоюзной переписи населения I959 г.

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Таблица 3

ЗАБОЛЕВАЕМОСТЬ ПОЛИОМИЕЛИТОМ В г. ТАШКЕНТЕ В 1950–1958 г.г. и в 1959 г.

Годы	месяцы												Всего	Годовой % к общему количеству случаев за 9 лет	% к общему количеству случаев за год в Уз. ССР	Показатель заболеваемости на 100.000 +)
	I	II	III	IУ	У	УI	УII	УIII	IX	X	XI	XII				
1950	4	3	5	2	5	6=)	4	5	I	2	3	2	42	9,9	79,2	
1951	3	0	2	0	0	I	2	0	2	I	5=)	I	I7	4,0	50,0	
1952	2	I	3	2	5	20=)	I8	7	4	2	0	2	66	I5,5	70,2	
1953	I	I	I	3	3	3	5=)	2	5=)	I	I	I	27	6,3	40,9	
1954	2	2	0	2	2	2	4	5=)	3	I	4	I	29	6,8	4I,4	
1955	5	0	0	0	0	6	6=)	2	4	6=)	5	5	34	8,0	3I,5	
1956	0	3	I	3	7	9=)	7	7	0	5	I	4	49	II,5	25,I	5,3
1957	2	I	3	6	3	5	I3=)	I2	4	7	6	I	66	I5,5	28,9	7,2
1958	5	2	4	5	II	I8	24=)	9	7	5	5	2	96	22,5	35,2	I0,5
Общее количество случаев за 9 лет	24	I3	I9	23	36	70	83	49	30	30	30	I9	426	I00,0		
%	5,6	3,I	4,5	5,4	8,4	I6,4	I9,6	II,5	7,0	7,0	7,0	4,5	I00,0			
среднее количество случаев за I год	2,7	I,4	2,I	2,6	4,0	7,8	9,2	5,4	3,3	3,3	3,3	2,I	47,3			
1959++)	3	0	I	3	2	37	250=)	I03	I6	5	I	2	423			40,0

Примечание:

=) Максимальное количество случаев за I месяц в течение соответствующего года.

+) Вычислено на основе данных Всесоюзной переписи населения 1959 г. /917.000 человек населения г. Ташкента/ Показатель за 1959 г. вычислен из расчета I.060.000 человек населения г. Ташкента, так как после переписи в состав города введено два новых ранее пригородных района /Калининский и Карасуйский/.

++) С июня показано количество случаев паралитического полиомиелита, зарегистрированных по датам заболевания /а не госпитализаций, как обычно/.

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Таблица 4

ВОЗРАСТНАЯ СТРУКТУРА ЗАБОЛЕВШИХ ПОЛИОМИЕЛИТОМ В г. ТАШКЕНТЕ В 1957, 1958 и 1959 г.г.

Возрастная группа		0–1 г.	1 г.	2 г.	3 г.	4–6 л.	7–9 л.	10–14 л.	15 и выше	Всего
Количество заболевших	1957 г.	10	25	11	7	5	4	4	0	66
	1958 г.+)	12	33	26	7	7	5	5	1	96
	1959 г.	71	166	68	46	23	12	7	2	395
% к общему количеству заболевших за год	1957 г.	15,2	37,9	16,7	10,6	7,6	6,0	6,0	0,0	100,0
	1958 г.	12,5	34,4	27,1	7,3	7,3	5,2	5,2	1,0	100,0
	1959 г.+)	18,0	42,0	17,2	11,7	5,8	3,0	1,8	0,5	100,0
Показатель заболеваемости на 100.000 лиц возр. группы	1957 г.++)	55	126	57	37	12	9	6		28=)
	1958г.++)	61	159	127	37	18	10	7		37=)
	1959г.+++)	297,7	696,1	285,2	213,1	37,6	19,7	6,5		118,5§)

Примечание: +) Разработана возрастная структура заболевших с I.VI. по 10.IX. /92% всех заболевших в 1959г./

++) Показатели высчитаны по данным до Всесоюзной переписи 1959 г.

+++) Показатели высчитаны на основе данных Всесоюзной переписи 1959 г. с учетом увеличения населения города после включения в его состав 2 пригородных районов.

=) Показатель на 100.000 населения до 14 лет включительно.

§) Показатель на 100.000 населения до 15 лет включительно.

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Таблица 5.

ЗАБОЛЕВАЕМОСТЬ ПОЛИОМИЕЛИТОМ В г. ТАШКЕНТЕ с I.П. 59 г. по 3.I.60 г. /23-53 недели/

Недели	23 I-7/II	24	25	26	27	28	29 x)	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53
Количество заболевших	5	5	8	14	86	40	78	69	57	87	18	19	9	6	3	1	3	1	-	2	2	1	-	-	-	-	1	1	-	-	2	-
Показатели заболеваемости на 100.000 до 15 л.	1,6	1,6	2,5	4,2	11,3	12,4	22,6	20,4	17,7	11,5	5,6	5,9	2,8	1,9	0,9	0,3	1,9	0,3	0,0	0,6	0,6	0,3	0,0	0,0	0,0	0,3	0,3	0,0	0,0	0,6	0,0

Примечание: x) вакцинация в конце 29 недели /19.УП./ и в середине 30 /28.УП./.

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Рис. 1.

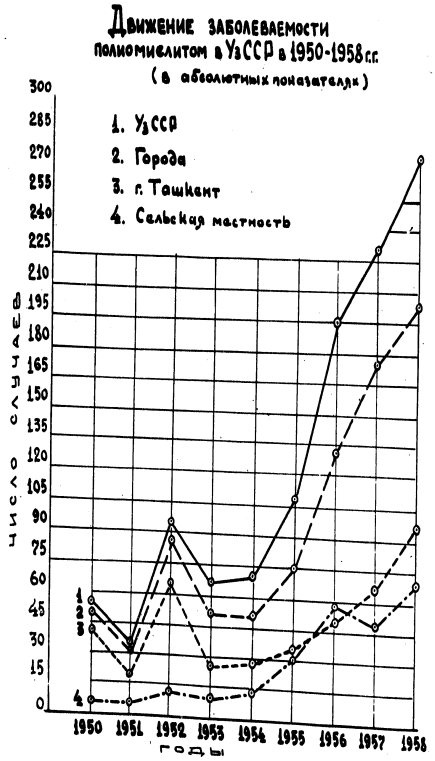

Рис 2.

1958-1959

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Рис 3.

Ежедневная заболеваемость полиомиелитом по г. Ташкенту с 1 VI по 13 IX 1959 г.

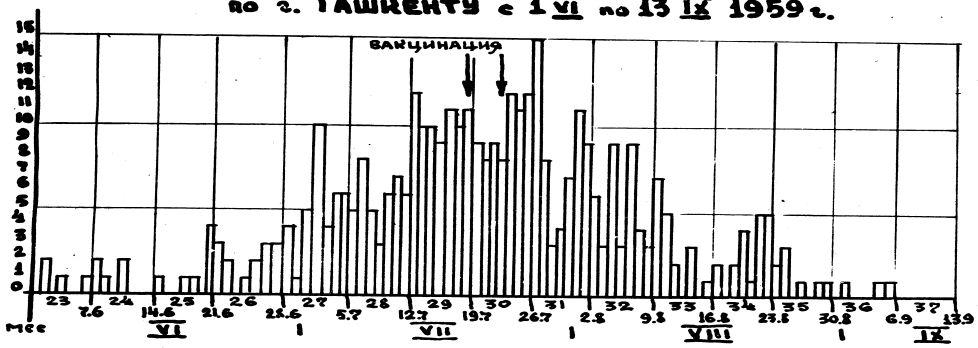

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Рис. 4.

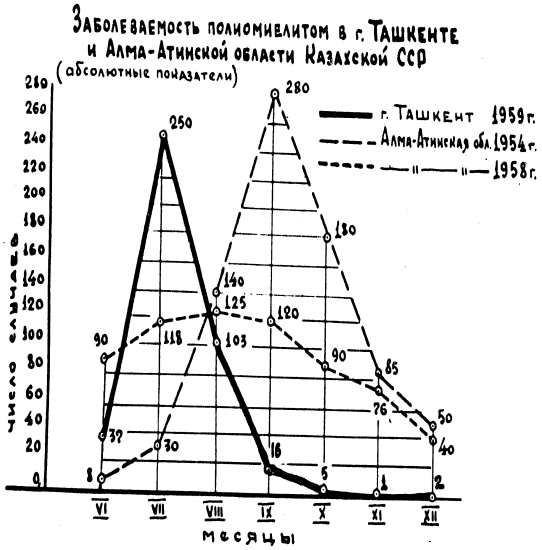

Рис. 5.

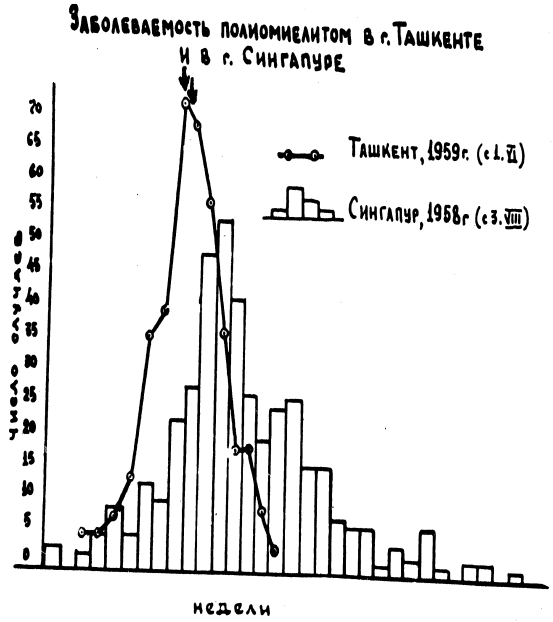

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Рис. 7.

Паралитический полиомиелит в г. Ташкенте в 1959 г.

(в относительных показателях на 100.000 детей до 15 лет)

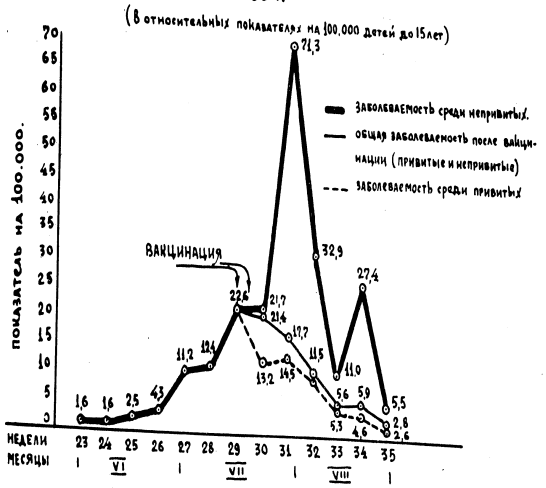
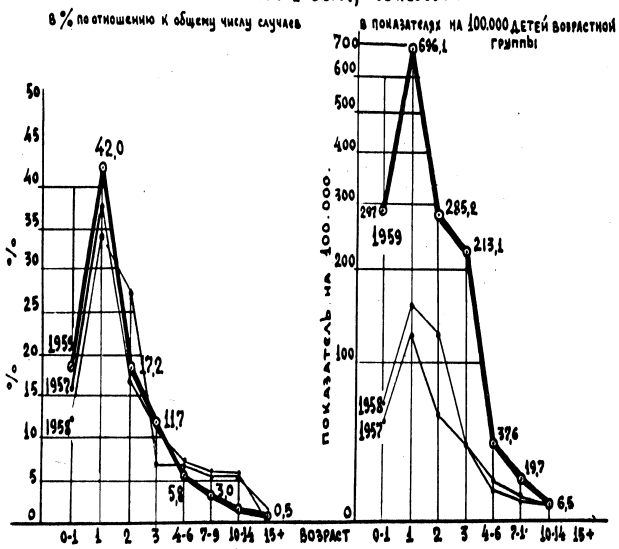


Рис. 8.

Возрастная структура заболевших полиомиелитом в г. Ташкенте в 1957, 1958 и 1959 г.г.



1958-1959

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ACADEMY OF MEDICAL SCIENCES OF THE USSR

INSTITUTE FOR THE STUDY OF POLIOMYELITIS

STAT

EPIDEMIOLOGICAL STUDY OF THE EFFICACY OF MASS IMMUNIZATION AGAINST POLIOMYELITIS WITH LIVE VACCINE IN THE LATVIAN SSR DURING 1959.

K.G.Vasiliev, E.V.Glinskaya, E.N.Kibitkina,

A.Ya.Khvatova, P.P.Khvatov / Riga/.

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Under the guidance of Prof. A.A.Smorodintsev large=scale immunization against poliomyelitis with live vaccine was carried out in the Latvian SSR during 1959 . The broadly organized vaccination was preceded by the study of live vaccine reactogenecity, which demonstrated its complete clinical areactogenecity, both with regard to neurological responses and to those provoked by infections of general nature.

The epidemiological situation in the republic at the outset of mass immunization looked as follows: Following the large epidemiological upsurge of 1955-1956 the poliomyelitis morbidity in 1957 showed a sharp decrease. But its level was, nevertheless, still higher than in the years of all previous interepidemical periods. The poliomyelitis morbidity factor in 1957 was as high as 9.0 /per 1000 000/. Sporadic cases of the disease were registered in most of the districts and cities of the republic. As distinct from the situation existing during the former interepidemic periods- in 1958 the poliomyelitis morbidity not only failed to show any decrease, but actually rose up to 10.1, and its level was on the par with that of 1948, the year distinguished by maximal poliomyelitis incidence in Latvia during the epidemical outbreak preceding the last one. The pattern of the disease, as before, retained its seasonal character, with the bulk of cases falling to August-October, whereby no less than 2/3 of all cases of poliomyelitis recorded during the year occurred in the months of the autumn and winter periods. Maximal incidence was observed among the children of junior age groups.

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Vaccination with killed vaccine after Solk, effected in many districts and cities of the republic in 1957-1958 failed to exercise any appreciable influence on the general poliomyelitis incidence. When analysing the epidemiological efficacy of inoculation with dead vaccine in Riga one could note that within the first six months following the second vaccination the incidence of the disease among the inoculated diminished by 4-5 times. But already 7-8 months thereafter the difference in the disease incidence in the vaccinated and non=vaccinated groups practically vanished. Thus, in the first six months of 1958 the poliomyelitis incidenceamong those subject to twofold vaccination after Solk in Riga during 1957 comprised 5.5, while among non=vaccinated it equalled-4.0.

Large=scale immunization against poliomyelitis with live vaccine was started in the Latvian SSR in April 1959. Vaccination covered 21 districts and 6 cities standing under immediate administration of the republican authorities. Inoculations were effected according to a scheme providing for twofold vaccination / first with the I type and second with -II and III types/. Single vaccination was applied to a total of 420.544 subjects, while the twofold one covered 367.000 persons. 22 districts were reserved as control. Districts and cities whose inhabitants were covered by immunization have their location in various parts of the republic. poliomyelitis cases therein were regularly recorded, both prior to the epidemic upsurge of 1955=1956 and thereafter. In this connection it is to be noted that here the intensity of the disease was even greater than in the districts serving as controls. Ordinarily, these districts and cities were responsible for a considerable part of all poliomyelitis cases registered in the republic. Thus, in 1954 the recorded propor-

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tion of the disease incidence constituted here 77%, in 1955 - 79%, in 1956-86%, in 1957 - 77% and in 1958 -80.4%.

At the time of mass immunization / April-May 1959/ two cases of poliomyelitis were registered among the vaccinated and three-in the control group. A thorough epidemiological and clinical examination of the diseased revealed the infection to have taken place either before inoculation of the live vaccine, or at the time when vaccination could not yet have exercised its effect.

Epidemiological surveyance of the vaccinated was commenced beginning from the 1st of June 1959,i.e. one month after immunization with the first type. In the processing of the material on the poliomyelitis incidence and in judging the efficacy of the live vaccine it were data of acute anterior poliomyelitis exclusively that served as a background for the study.

The first factor that invites particular attention while analyzing the poliomyelitis morbidity in the Latvian SSR during 1959 is a considerable decline of the poliomyelitis incidence rate in the republic. Thus, if we take the incidence of acute anterior poliomyelitis in 1957 as representing 100, its rate in 1958 will go as high as 170.8%, while in 1959- drop down to mere 29.1%. But it were by far not all districts of the republic that benefited from the reduction in the incidence of the disease. This can be clearly seen when comparing seasonal poliomyelitis morbidity curves for 1957,1958 and 1959 separately for territories covered by the vaccination and those outside of it. The decrease in the incidence rate in 1959 was due to a sharp decline of the number of cases in districts covered by the vaccination. At the same time the poliomyelitis morbidity in con-

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trol districts /those where no vaccination with live vaccine has been effected/ remained approximately on the level of 1957-1958. But inasmuch as the intensity of the poliomyelitis spread in the area covered by vaccination was appreciably higher, / from 77 up to 86% of all recorded cases of the disease in the republic/ it is but natural that the decline in the incidence rate in these districts and cities brought with it also a sharp reduction in the rate of this disease throughout the republic. This decrease for the entire territory of the republic , however, did not arrive at once. During the first six months of 1959 the morbidity rate kept on the same level as in analogous periods of 1957-1958, and it was only in the third quarter of 1959, i.e. after vaccination, that the incidence of the disease fell considerably. To this it should be added that it is just the third quarter when seasonal upsurges of poliomyelitis ordinarily occur in Latvia, and the absence of such a rise in the incidence rate in 1959, for the first time since several decades,would be completely inexplicable, if the influence of the preliminarily conducted immunization should be denied.

The reduction of the morbidity rate following inoculation of live vaccine becomes especially apparent when analysing the poliomyelitis incidence in districts and cities subjected to immunization.

The incidence rate of acute anterior poliomyelitis on the territory covered by inoculations with live vaccine in June, August and September 1959 decreased by 9 times, as compared with the same months of 1957, and by 21 times, if contrasted with analogous periods of 1958. Very demonstrable are also comparative figures for the poliomyelitis incidence in the vaccinated and

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non=vaccinated groups.

For the period of seven months, beginning from the 1st of June and ending with 31st of December 1959 a total of 18 subjects fell victims to the acute anterior poliomyelitis in the Latvian SSR. Of these -1 was from among the vaccinated, 3- from the group of non=vaccinated in the area covered by immunization and 14 came from the territory outside the vaccination zone / external control/. The number of diseased within the groups subject to vaccination after Salk /threefold inoculation/ - included one immunized with live vaccine and another one from among those not covered by it.

For the purpose of comparison and statistical analysis data were gathered relative to the incidence of acute anterior poliomyelitis among vaccinated and non=vaccinated groups of population in the age bracket of up to 14 years.

The intensity rate / 1 : 100 000/ in these groups was: for the vaccinated - 0.4; for non= vaccinated /internal control/- 0.7 and for the non=vaccinated of the external control-6.5.

The effectivity indices, when comparing the incidence rates for the groups of vaccinated and for those of external control, are as follows: the effectivity index- 16.2, the effectivity factor -93.8%; when compared with the incidence rate in the group of internal control these figures are- 1.7 and 41.1%.

The determination of the statistical significance of the effectivity index with the aid of the criterion X^2 / after Finni, 1957/ shows that the difference in the morbidity rate in the groups of vaccinated children, as contrasted to those of external controls, is very significant / X^2=11.88/.

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STAT

THE STUDY OF REACTOGENIC PROPERTIES OF LIVE VACCINE AGAINST POLIOMYELITIS IN RIGA IN 1959.

K.G.Vasiliev, E.N.Glinskaya / Riga/

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Withk the permission of the Ministry of Public Health of the Latvian SSR in January-March 1959 an experiment was staged in Riga the aim of which was to study reactogenic properties of live vaccine against poliomyelitis, prepared by the virusological department of the AMS USSR institute of Experimental Medicine. The experiment was conducted under the guidance of Prof. A.A. Smorodintsev. From the 20th till 30th of January 1959 a total of 9.657 children of pre=school and school age were subjected to immunization with live vaccine in Riga. All of the vaccinated children attended establishments for children and schools in one of the selected city districts of Riga. In each one of these establishments and schools a group of non=vaccinated children was set apart / internal control/, which comprised no less than 30% of the total number of children in the establishment. In addition to this, with the view of conducting proper observations and comparative studies a large group of non= vaccinated children, counting 4.362, in the same age bracket was selected in another district of the city. Vaccination was realized by parenteral administration of monovalent and polyvalent vaccines in a spoonful of sugar syrup. The immunization of pre= school children was effected according to a threefold scheme with monovalent vaccines of the I,II and III types, introduced in a different order of succession, while that of school children was organized on the basis of twofold administration: the first one with the vaccine of the I type and one month afterwards - with polyvaccine comprising the I and II types.

From among the children under observation in 1958 Salk vaccine was inoculated: in the group of immunized -to 83.5%, in the group of non=vaccinated in the children bodies covered by immunization / internal control/-to 84.6% and in that of the external control - to 82.1%.

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Observation of pre=school children and of those attending schools, which lasted for 76 and 73 days respectively, was conducted by physicians of the corresponding establishments for children. Observations covering the vaccinated subjects succeded in establishing clinical areactogenecity of live vaccine with respect to neurological reactions and response to general infections. Among the total of 9.657 primarily vaccinated children in Riga only 13 instances of short=spaced reaction were registered which might be associated with the vaccination. This reaction was manifested in elevated temperature for a period of one-two days, nausea, vomiting, languor, all of them appearing on the first day upon vaccination and then disappearing completely.

The study of the disease incidence in the groups of vaccinated and non=vaccinated / internal and external controls/ revealed that the immunization did not exert any deleterious influence upon the general morbidity among the vaccinated. The morbidity rate according to principal nosological groups among the vaccinated did not exceed this rate in the category of non=vaccinated. The period of the studies relative to the reactogenecity of live vaccine coincided in Riga with a considerable outbreak of asiatic influenza. Individual outbreaks of this disease were noted also in establishments for children, where , prior to the epidemy, inoculation with live vaccine against poliomyelitis had been effected. However, as proved by observations, vaccinations had no aggravating effect upon the course of the influenza infection. By its severity the clinical course of influenza in the vaccinated children differed in no way from that in the non=vaccinated ones. Within the period of observation among the vaccinated were also registered cases of measles, diphtheria, scarlet fever and of other infectious diseases. All these

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patients were duly hospitalized and, according to the expert opinion of specialists, the course of the disease observed in them showed no noticeable deviations from the ordinary clinical picture specific to these affections.

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EXPERIENCE WITH MASS IMMUNIZATION OF CHILDREN IN PSKOV AND NOVGOROD REGIONS WITH ATTENUATED LIVE POLIOVIRUS VACCINE

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One of the most promising means to reduce poliomyelitis incidence and, possibly, to eradicate entirely this disease is the use of live vaccines prepared from attenuated poliovirus strains.

Experimental investigations and clinico=epidemiological observations made by A.Sabin and collaborators, Kh.Koprovsky and collaborators, A.A.Smorodintsev and collaborators, M.P. Chumakov and collaborators made certain the innocuousness and immunological efficacy of live vaccines, this having created firm pre=requisites for a broad trial of this preparation under epidemiological conditions.

This communication lists preliminary results of a mass immunization of children with live vaccine effected in 1959 on the territories of Pskov and Novgorod regions.

The charge over the procedural aspects and actual effectuation of vaccination was taken over by the Leningrad Pasteur Institute conjointly with the public health agencies of the Pskov and Novgorod regions. The processing and interpretation of the materials obtained were done at the the laboratory of the Pasteur poliomyelitis institute and at the virological division of the AMS of the USSR IEM.

To perform vaccination a preparation comprising liquid vaccine prepared from attenuated Sabin's strains at the virological division of the AMS of the USSR IEM and at the AMS USSR poliomyelitis institute was used.

The vaccine was administered perorally in doses of 2 drops droplets per spoonfull of a 5% sugar syrup. The minimal amount of the vaccinal virus per one taking comprised 100 000 $TCID_{50}$

With the view of attaining maximal effect of immunization in the current season we limited the latter to two vaccinations:

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the first inoculations with the vaccine of the I type were effected on the 15-25/VI-59; the second set of inoculations was made with the vaccine of the II and III types during 15-30/VII-1959. By the I of August 1959 a total of 370 815 subjects were immunized.

I. The Age Pattern of the Vaccinated.

As seen from the data in Table I the age pattern for the vaccinated proved uniform for both regions (each age group comprises 24-27% of the sum=total of the vaccinated).

To arrive at an objective assessment relative to the efficacy of the vaccination of major importance is the extent to which different age=groups of the population are covered by inoculations. The figures listed in Table 2 are illustrative of the high percentage attained in covering with immunization the most susceptible categories of the population (75-85%), both in Pskov and Novgorod regions. As seen, over 2/3 of the susceptible population on these territories were inoculated with live vaccine.

II. Harmless Nature of Immunization with Live Vaccine

One of the most important conditions determining the possibility of mass employment of live poliovirus vaccine is its innocuousness to humans. In this connection of considerable interest are the data on the polio=incidence among vaccinated and non=vaccinated groups of the inhabitants at the time of immunization and in the course of the 1st month upon its termination, i.e. during periods when the attenuated virus shows most intensive multiplication in the intestines of the inoculated. Tables 3 and 4 carry lists of persons who fell victims to the disease in Pskov and Novgorod regions in the course of the months of June and July. From these one can see that dur-

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ing the first half of June, i.e. before immunization was started a total of 9 cases of the disease had been registered (an index of 3.9 per 100 000 of inhabitants). A substantial proportion of this group was represented by spinal forms of the disease and, etiologically, was due to the I type of the virus.

At the time of mass poliovirus vaccinations (the second part of June) the frequency of the disease remained on the same level (9 cases with the index of 3.9 per 100 000 of residents). Remarkable is also a high proportion of severe paralytic forms. Negative results of laboratory investigations obtained for a number of patients in this group, is apparently, due to the fact that the materials for laboratory analyses were obtained long after the onset of the affection. All the cases recorded in the second half of June and in July occurred in immunized persons, who comprised 84-86% of the entire population in the age=bracket of up to 15 years. Along with this not a single polio=case was noted among subjects in close contact with the vaccinated (they comprised 60 000 in Pskov and Novgorod regions). Consequent upon the analysis of each one of the above=cited 12 polio=cases among the vaccinated, one can distinguish 4 individual groups of patients:

1). 9 cases (NN 1-9), which occurred shortly upon vaccination (1-5 days), this giving reason to consider them as a result of superimposition upon the vaccination of a formerly developed infection. This is also confirmed by the data of epidemiological investigations, which revealed that in 2 out of 9 instances (NN 3,7 - patients D-va and G-va) the disease was due to contacts with a non=vaccinated child (see table 3, No 4-patient P=v) afflicted with the disease 9-12

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days prior to the initiation of mass immunization, these contacts being effected either in the establishment for children or domestically.

2) In 2 cases (NN 11,12-patients M=ova and K=v) the laboratory examination traced the origin of the disease to the etiological part played by the virus of the II type, which was not introduced to children.

3) 1 case came up on the 17th day after a single vaccination (N 10-patinet B=v). This was diagnosed as a " pontal form of poliomyelitis" and occurred in an adolescent aged 14 . According to O.A.Rodshtein from the laboratory of the Pasteur Polio=Institute, most often than not, virological investigation of pontal forms in children of pre=school and school ages renders negative results, which enables it to suspect some other / not poliomyelitic/ origin of such cases.

It should be emphasized that all pontal forms registered within the same period in non=vaccinated children were observed among subjects of the junior age=group(below 3 years), where, as stated by the same author, the percentage of laboratory confirmations of the diagnosis was considerably higher.

Hence, the analysis of polio=morbidity at the time of mass immunization with live vaccine permits it to arrive at the following conclusions:

1) In the weeks immediately following vaccination-immunization failed to bring about any reduction in the incidence of the disease.

2). No cases of the disease could be registered, which might be associated with the use of live vaccine.

3) The harmlessness of the vaccine for the persons contacting the vaccinated finds its confirmation in the absence

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of infection cases among the non=vaccinated groups of residents.

On the Reactivity of Vaccinations.

Here we present the results of medical observations of the vaccinated, carried on for 7 days after immunization. They were effected by the medical staff of creches and kindergartens, as well as by district physicians, whereby all the data obtained were entered onto special forms, which were then subjected to statistical processing at the Pasteur Institute. Altogether 366 685 froms were studied. The end=results are presented in a series of tables.

Table 5 characterizes the number of reactions observed within each age=group.

Most often (in 0.8-1.0% of cases) the reactions were noted in children of the junior age=group / up to 2 years/. In senior age=groups there took place a gradual decline in the frequency of reactions down to the index of 0.2% for the children aged over 7. On the whole, the total number of reactions did not exceed 0.4%. The nature of the reactions actually observed is reflected in the following table.

As illustrated by table 6 of the most frequent occurrence was temperature rise (0.25-0.27%), of lesser frequence were gastro=intestinal disorders (0.16%), while the least frequent turned out to be nervous reactions,(predominantly headache), along with those of allergic nature, such as, rash . There was not one case of paralysis or paresis of the upper or lower extremities . The vast majority of reactions were registered in the first 2 days following vaccination and lasted for 24-48 hours.

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Indices obtained by us upon statistical interpretation of materials are corroborated by the data of daily thermometry and of medical examinations of over 4500 children aggregated in organized collective bodies, effected for a period of 1 month before and after vaccination. With all this, reactions (elevated temperature, gastro=enteric disorders, etc) were observed only in 0.37-0.39% of cases shortly after the vaccination, and much less frequently (0.07-0.09%) in the same children, one month prior to or following the immunization.

Thus it can be stated with full measure of assurance that at the time of immunization with live vaccine there actually did occur various types of reactions in the vaccinated children. But, taking due account of the fact that the vaccination campaign was effected in summer months and it coincided with the seasonal rise in the indidence of intestinal affections, they cannot be with certainty referred to as after-effects of the vaccinations, as such.

The possibility is not excluded that a substantial number or recorded temperature and other reactions have no immediate connection with the action of live vaccine, but are rather to be regarded as the result of some parallel running mild affections of diverse nature, common for the very young.

On the other hand, even accepting the specific nature of the reactions observed, their insignificance gives ground to infer that the immunization with live poliovirus vaccine has an extremely low reactogenecity.

Inasmuch as during mass immunization of children with live poliovirus vaccine inoculated could be also those of them who were in the incubation period in connection with various infectious disease- it was of interest to determine

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the course of these latter in the vaccinated and non=vaccinated subjects. With this aim in view we have examined 963 histories. The severity of any one of the affections was estimated conjointly with the clinicians. The final results are given in table 7. As seen from the data included in this table the distribution of mild, moderate and severe forms of the diseases proved to be quite uniform, both in the vaccinated and in non=vaccinated groups. Thus, it can be said that the live vaccine does not aggravate the course of any other infectious disease, this being of great significance for the setting up of contra=indication to vaccination.

On Immunological Efficiency of Vaccinations.

Immunological indices for the residents with respect to the poliovirus are characterized by the results of an examination of 564 sera obtained from diverse age=groups before immunization and of 524 sera collected from inoculated children 1-2 months after completion of vaccinations.

A considerable proportion of these groups is represented by permanent categories of persons examined repeatedly prior to and after immunization. The sera were investigated for the presence of virus=neutralizing antibodies in a color test against 100 CPD of each virus.

Table 8 indicates the number of subjects having no antibodies to the I,II and III types of poliovirus, in each age bracket.

From the table one can see that before vaccination this group was proportionately high among children aged up to 2/63 82% years, quite considerable among children of 3-4 years /31-60%/ and then declined markedly with the increasing age, retaining

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its high level only with respect to the II type of the virus.

The cited data permitted to estimate the probable number of susceptible subjects within the sum=total of the immunized with each type of the vaccine. The corresponding indices listed in the right half of the table are characteristic of the high numercial proportion of that stratum among the residents of the Novgorod and Pskov regions which was susceptible to poliomyelitis before the introduction ov vaccination.

Below are given the results of examinations, which covered 128 subjects repeatedly investigated 1-3 months after vaccination / table 9/.

The line of totals in the table shows that inoculations of live vaccine were attended by intensive accumulation of antibodies to the first type of the virus in 80% of the examined (102 persons), to the II type - in 95% (128 persons), and to the III type - in 64% (104 persons).

Thus, the highest percentage of positive results was revealed in the instance of the II, and the lowest- in that of the II type of the virus. The last circumstance cannot be explained by the defects in the vaccination technique, since the whole of the above group was subject to inoculation with a divaccine of the II and III types. The absence of immunological shifts to the III virus type in children,who responded positively to the introduction of the II type virus, is, possibly, caused by the interfereing effect of the latter.

If, further, the immunological indices after vaccination are considered in relation to the initial antibody titre one can disclose an interesting fact: in the group of seropositive children / titres before the vaccination -4-16/ immunization with live vaccine was accompanied by an amassment

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of antibodies in a higher percentage of instances than this was the case with seronegative children.

Account should be taken of the fact that the last group includes, chiefly, children of the junior age bracket. One may presume that the above age=groups include refractory subjects. One of the reasons for such refractoriness may be the interfering influence of some other infection agents (viral and microbial/, very often found in the intestines of small children.

In general, repeated examinations of the vaccinated children tend to confirm the high immunological efficacy of the preparation used for immunization.

IV. Preliminary Data on the Epidemiological Efficacy of Immunization with Live Vaccine

The present work includes only preliminary data depicting the influence of vaccinations on the polio=incidence, which embrace the results of a 7-months observations of the vaccinated and non=vaccinated groups of the population. An analysis of the polio=incidence according to individual months for a number of years (1955-1958) discloses distinct rises of the morbidity=rate, with their maximum in July=August, this being particularly characteristic of the pskov region. Mass immunization with live vaccine in June 1959 was accompanied by a substantial change in the seasonal curve: the growing frequency of polio=cases in the period previous to the vaccination was, further, not attended with the rising incidence in July=August, as could be observed, for instance, in 1956 (table 10) Quite the contrary, during the whole of the period under investigation (July-November) the morbidity=rate was rather low.

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Thus, there is a marked change in the seasonal incidence curve , typical for poliomyelitis.

This is also corroborated by confronting semi=annual sum=totals of polio=frequencies.

As can be noted from the table the incidence in the second half of the year, for a number of years, constituted the bulk of the total annual number of polio=cases.

These rations, characteristic of poliomyelitis, experience an abrupt change in 1959, following the vaccination. Furthermore, in the second half of the year the number of polio=cases was appreciably lower than in the first one. One may suppose that this was due to the development of collective immunity resulting from vacciantions. This presumption is confirmed by a separate monthly analysis of morbidity among the vaccinated and non= vaccinated subjects.

As can be seen from the materials included in table 12 already in July 1959 there could be revealed certain differences in the morbidity indices for the vaccinated and non=vaccinated groups / indices 0.5 and 2.8/; in August these differences became still more clear=cut / indices 0.5 and 8.5/ and later on were again confirmed also in October, December and February / indices-1.0 and 5.6; 1.0 and 8.5; 0 and 5.6/. During the whole period of 7 months (from the 1=VII-59 till the 1/III-60) the number of cases revealed among the vaccinated comprised 11 and among non=vaccinated -9, which, taken in percent per 100 000 of the population, gives indices amounting to 32.5 and4.5. The efficiency index, calculated on the basis of these figures is equal to 7.2.

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According to statistical analysis the mean error of summary indices of the morbidity=rate, as well as the error in their difference lie within the limits of permissible deviations, this permitting to consider the disclosed differences to be fully authentic.

Hence, within the period of observation there could be registered a 7-fold reduction of polio=incidence among the vaccinated, which testifies to the efficacy of the preparation employed by us. The efficiency of immunization with live vaccine is also illustrated by the figures contained in table 13, which lists the polio=frequency according to individual clinical forms.

As seen in the table the severest spinal forms of the disease were recorded only in non=vaccinated children and could not be found among the subjects of the non=vaccinated group. Along with this was a singular phemomenon was marked for affections diagnosed as " pontal form of poliomyelitis"; viz; morbid cases of this nature could be observed only in non=vaccinated children aged up to 4. At the same time the pontal form of the disease in children of senior age=groups was characterized by ratios equal to, both the vaccinated and non=vaccinated groups. Notice should be taken of the fact that the results of virological and serological investigations in these cases were invariably negative. As shown by Rodschtein and Pratusevich, affections among elder children and adolescents diagnosed as a"pontal form of poliomyelitis" differ from typical forms of poliomyelitis by a number of cardinal signs, which gives ground to suspect a different / non=poliomyelitic/ origin underlying these cases.

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In this report we deem it possible to emphasize yet another feature peculiar to this group, namely,- immunization with live poliovirus vaccine, apparently, does not influence its numberical composition , at the same time markedly reducing the number of other polio=forms.

This will , possibly, serve as one more confirmation of the hypothesis about non=poliomyelitic nature of isolated pareses of facial nerves in children of senior age=groups and in adolescents.

Considering that all polio=cases of this nature in the the vaccinated observed over the period under examination /9 cases/ occurred within this very group it may be suggested that that the factual efficacy of immunization with live vaccine estimated in the course of the further study of authentic polio=cases would be higher than that indicated by us in this report.

CONCLUSIONS.

1. Vaccination with live poliovirus vaccine, which covered 370 000 children proved complete innocuousness of the preparation under study.

2. The live vaccine possesses low reactogenecity and does not influence the course of other infectious diseases.

3. Experience established a considerable degree of immunological efficacy of the preparation under study. At the same time some subjects showed refractiveness to the introduction of individual components of live vaccine. The actual number of such refractive persons and the possible means of overcoming the said refractiveness demand further profound investigations.

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4. On the territories covered with vaccinations there could be noted a marked decrease in the seasonal curve of polio=incidence.

5. Preliminary information now on hand testifies to a considerable epidemiological efficiency of immunization with live poliovirus vaccine.

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TABLE I

Age Pattern of the Immunized with Live Poliovirus Vaccine.

Age-groups	Pskov Regions — Vaccinated			Novgorod Region — Vaccinated		
	I type	II type	III type	I type	II type	III type
9 months-3 yr:	4y2y2	42182	42182	41433	4085y	40859
	24.9	24.9	24.y	25.6	26.1	26.1
4-6 years	456yy	39553	39553	3y990	39073	39073
	23.1	23.4	23.4	24.8	25.0	25.0
7-9 years	47804	41757	41757	37y60	36551	36551
	24.2	24.7	24.7	23.5	23.4	23.4
10-15 years	55039	45484	45484	42384	39y58	39y58
	27.8	27.0	27.0	26.1	25.5	25.5
Total :	1y7834	168y86	168y76	161769	156441	156441
	100.0	100.0	100.0	100.0	100.0	100.0

N O T E : For each age-group is indicated the number of the vaccinated and the percentage of the total number of subjects immunized with the given type of vaccine

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T A B L E 2.

The Coverage with Live poliovirus Vaccine Immunization of Different Age Groups.

Age-Groups	Pskov Region				Novgorod Region			
	Total population	Vaccinated I type	Vaccinated II type	Vaccinated III type	Total population	Vaccinated I type	Vaccinated II type	Vaccinated III type
9 months-3 years	56425	49292	42182	42182	48147	41438	40859	40859
		87.4	74.8	74.8		85.6	84.4	84.4
4 - 6 years	52225	45699	39553	39553	43960	39990	39073	39073
		87.5	75.7	75.7		91.0	88.8	88.8
7 - 9 years	56188	47804	41757	41757	43513	37960	36551	36551
		85.1	74.3	74.3		87.2	84.0	84.0
10-15 years	68249	55039	45484	45484	50703	42381	39958	39958
		80.6	66.6	66.6		83.6	78.8	78.8
T O T A L :	233087	197834	168976	168976	186593	161769	156441	156441
		84.9	72.4	72.4		86.7	83.8	83.8

N O T E : The table lists the numbers of vaccinated and percentages of each age-group covered by immunization.

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DYNAMICS OF EXCRETION OF THE THREE TYPES OF VACCINE VIRUS IN VACCINATED CHILDREN AND THEIR CONTACTS. INVESTIGATION OF PROPERTIES OF VIRUS ISOLATES.

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When mass vaccinations with live poliovirus vaccine were started in the Soviet Union for the first time (Estonian SSR) complex investigations of problems concerning use, properties and effect of the live vaccine was undertaken (Chumakov, I960; Chumakov et al., I959).

Oral immunization with live attenuated poliovirus reproduces natural asymptomatic intestinal infection resulting in development of resistance to the corresponding type of the virus. Implantation and multiplication of the virus in the intestinal tract constitutes one of the important aspects of vaccination process.

The main method of evaluation of vaccine virus multiplication in the intestinal tract consists in virologic examination of stool samples from the vaccinated. Using this method first investigators of live vaccine (Sabin, I956,I957; Koprowski et al.,I956; Horstmann et al.,I957) found out the main principles of multiplication of different poliovirus types in the human intestinal tract.

In studing the dynamics of vaccine poliovirus multiplication in the intestinal tract and possibilities and patterns of their contact spread we also used virologic methods for testing stools.

This paper presents the results of our work.

MATERIALS AND METHODS

In a closed institutional community of children under 3 years of age (I74 children) vaccination was carried out with live

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monovalent poliovirus vaccine obtained from Dr. A.B. Sabin (attenuated type I LSc, 2ab strain; type II P 7I2, Ch, 2ab strain and type III Lean, I2 a_Ib strain)*

On February 4, I959 we gave a fist feeding with type I vaccine, followed 28 days later (March 5) by a second with type III vaccine, and another 38 days later (April I0) by a third feeding with type II vaccine virus. The vaccine was given in two drops (about I00 000 TCD_{50}) of I : I0 virus dilution on a piece of bread or cake followed by water or in a spoonful of sweetened water or sugar syrup (for youngest children). All children were divided into groups of 8 to I2 persons, and in each group two to four children were left unvaccinated.

Stool specimens were collected from all children at 23 days and I day before vaccination and then regularly twice weekly for 4 months after the first feeding. Ten per cent suspension by weight prepared from stools was centrifuged at 4500 rpm for 30-45 minutes, and the supernatant was treated with antibiotics and stored in a frozen state until use.

Virologic investigations (virus isolation, titration and identification) were carried out in rhesus kidney cell tube cul-

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tures. For virus isolation primary inoculation of cultures and one additional passage were done.

For titrations IO-fold dilutions of the original stool suspensions were used. Each dilution was tested in four tube cultures (0.2 ml per tube). 50% end point was calculated after Reed and Muench. Titration results presented below are expressed as number of TCD_{50} per I.0 gm of feces. For virus identification homotypic hyperimmune rabbit sera were used.

A number of identification and titration tests was carried out in bottle tissue cultures under agar overlay (plague method).

Some virus isolates from stool suspensions were subjected to tests for t and d characters (marker method).

Testing for the t character consists in simultaneous titration of the virus at $36^{o}C$ and $40^{o}C$. It has been shown (Lwoff A. and Lwoff M., I959; Sabin, I959) that attenuated poliovirus strains multiply better, that is, reach higher titers, at lower temperatures. Virulent strain multiply equally well at $36^{o}C$ and $40^{o}C$ (or slightly more extensively at temperatures over $36^{o}C$). Based on this principle the index EOG (efficiency of growth) was suggested for definition of attenuation. It is expressed as difference of logarithm of virus titers at $36^{o}C$ and $40^{o}C$. Benyesh-Melnick and Melnick (I959) use an additional definition of strain: ratio of the EOG of the strain being tested to the EOG of reference attenuated (vaccine) virus of the same type. With the EOG value of 0.75 a strain is considered to be attenuated (t strain),with the value of 0.75-0.30 to have an intermediate degree of attenu-

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ation ($t^{\pm}$ strain) and with the value of 0.29-0.00 a strain is considered to be virulent (t^{+} strain). In our Tables the EOG and the ratio of the EOG of the strain tested to the EOG of the reference attenuated (vaccine) virus are referred to as "t deficit" and "t coefficient", respectively.

Testing for the d character is based on the lack of the capacity of attenuated poliovirus strains to produce plagues under agar overlay containing a reduced sodium bicarbonate concentration (0.II per cent). Virulent strains possess a better capacity for growth under such an overlay. Both attenuated and virulent strains give maximum titers under agar overlay at high bicarbonate concentration (0.44 per cent). The method of testing the d character was developed by Vogt, Dulbeco and Wenner (I957) and modified by Hsiung and Melnick (I958). Attenuation by the d character is defined by the EOP (efficiency of plating) and additionally by the ratio of the EOP of the strain tested to the FOP of the reference vaccine virus. The EOP value and the EOP ratio are calculated in the same way as for the t character. d, d^{*} and d^{+} characteristics correspond to numerical limits of the t character (Benyesh-Melnick and Melnick, I959). In our Tables the EOP values and the EOP ratios are referred to as "d deficit" and "d coefficient", respectively.

In parallel with virologic studies investigations of immunologic response of children by pH color tests were carried out (Dobrova, I.N.). These serologic investigations served as a basis for selection of study the population, and helped to evaluate vi-

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rologic findings. The data presented in this paper refer to children excreting no virus before vaccination.

Results

Data on the implantation of vaccine viruses of all the three types in the intestinal tract are shown in Table I.

For detailed study of the dynamics of vaccine virus multiplication in the intestinal tract we used specimens both from triple negative and tripe-positive children. Fig.I shows individual curves of each type of vaccine virus excretion both in serologically negative and serologically positive children. Summary curves illustrating the process of multiplication and replacement of viruses on consecutive vaccination with types I, III and II polioviruses are also shown.

Of 9 immune chldren tested 7 had not been vaccinated with the killed vaccine and had acquired antibody as a result of natural latent infection.

We compared the capacity of different types of virus to implant and multiply in the intestinal tract of non-immune and naturally immune children.

Type I vaccine virus was established and multiplied in all the chldren of both groups. The duration of its excretion, however, was much shorter in the immune compared to that in the non-immune children. It is seen in fig.I and Table 2 that the immune chldren ceased to excrete the virus between I2 and I8 days after vaccination while most of the non-immune children continued to excrete

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the virus up to 29 or 33 days.

The ratio of positive (virus-containing) to negative fecal specimens for the maximum period of virus excretion (33 days) in the non-immune group was 3.5 : I. The corresponding ratio in the immune group for the maximum period of excretion (I2 days) was 0.78 : I. Average titers of the excreted virus were approximately equal at 6 days after vaccination in both groups, but were much lower in the immune group at 2, 9 and I2 days. Thus, in the immune children the excretion of virus was not only of shorter duration, but also less extensive.

When the children fed type III virus were tested, all of them were found to be susceptible to this virus. We observed no significant differences either in the duration or in the amount of the virus excreted both by the immune and non-immune children (fig.I).

Examination of children fed type II vaccine virus demonstrated the difference in the number of susceptibles in the immune and non-immune groups. It is seen in Table I that of the ten non-immunes one child excreted no virus in any of the six specimens tested (for 26 days). Of the 9 immune children four excreted no virus in any of the 4 to 5 stool speciments tested (26-40 days postvaccination). Results of tests with stools from type II excretors (fig.I) suggest a lower extent of virus multiplication in the intestinal tract of the immune children, but the number of the immune excretors tested (3 persons) is too small for final conclusions.

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We also studied the possibility of contact spread of vaccine in the community. Fot this purpose stool speciments from children fed no vaccine virus but being in close contact with the vaccinated were tested.

All the IO unvaccinated contacts who were in this institution during vaccination with type I vaccine virus, excreted the same virus. Fig.2 shows individual curves of type I virus excretion in contacts.

Of 4 contacts examined during the period of type II virus vaccination one excreted this virus (fig.3).

During type III virus vaccination one contact was examined virologically. Three stool speciments collected from this child contained type II poliovirus. Titrations of the stool isolates were not done.

The problem of possible reversion of neurovirulence of attenuated strains after multiplication in the intestinal tract of vaccinees and after consecutive passages through the intestinal tract of contacts is very important in large-scale vaccinations with live poliovirus vaccines. For a long time investigators could determine neurovirulence of this or that poliovirus strain only by inoculation of monkeys;the results being evaluated according to a scale suggested by Sabin. The method of markers (t and d characters, in particular) developed recently seems to permit evaluation of the extent of attenuation by a more convenient method (see "Materials and methods")

We tested a group of type I poliovirus strains isolated from

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vaccinated and contact children at different times after vaccination and contact for the t and d characters.

Fig. 4 shows the general pattern of type I virus excretion in children from whom strains tested for these characters were isolated. Shaded are the samples which were the source of strains tested. Tests were made with tissue culture fluid of the first passage of the respective strains. The results of the tests are presented in Tables 3 and 4.

DISCUSSION

The dynamics of vaccine poliovirus excretion in vaccinated immune and non-immune children and their contacts has been studied. The frequency of vaccine virus implantation and multiplication in the intestinal tract of vaccinated and their contacts was found to be high. We noted a difference in the duration of type I virus multiplication in the intestinal tract of the immune and nonimmune children. The duration was much shorter in the immunes. The amount of the virus excreted by the immune children was smaller than that excreted by the nonimmune children. Sabin's data (1959) show that type I vaccine virus given repeatedly (one year or more after a first feeding) can establish in the intestinal tract of children possessing homologous antibody. Cases of repeated establishment, however, were observed by Sabin rather rarely, with the duration and the amount of virus excreted being considerably less than in primary immunization.

In studying cases of reinfection with type III vaccine poliovirus Sabin found that repeated ingestion of the virus rarely

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leads to its implantation in the intestinal tract. In cases of repeated implantation virus multiplication was less extensive and of shorter duration. Fig.5 shows the results of two observations made by Sabin.

We did not observe any significant difference in the duration and the amount of type III virus excreted by the immune and non-immune children. Similar results for type III (and also type II) virus were obtained by Horstmann (personal communication). Differences in individual susceptibility to repeated infection with type III virus accounting for the observed differences in the results may be related to the time of previous infection or vaccination, to antibody levels and to the extent of local intestinal resistance. In selection of the immune group of children we took into account only the presence or the absence of antibodies, but not their levels. It should also be remembered that in Sabin's observations one and the same (attenuated) virus strain was fed both primarily and repeatedly. The children whom we examined had acquired immunity as a result of latent infection with a naturally occurring strain and were reinfected with an attenuated virus.

Implantation and multiplication of all the three types of vaccine viruses in the intestinal tract of contacts which we observed confirms the possibility of immunization with live poliovirus vaccine through contact which is in agreement with data obtained by A.A. Smorodintsev (1959) who observed dissemination of vaccine virus in an unvaccinated community to which children vaccinated with live poliovirus vaccine shortly before their arrival came.

Tests for the t and d characters demonstrated that strain

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isolated from stools of the vaccinated and their contacts both at early days and 3 to 4 weeks after vaccination retained the properties of attenuated strains. One strain isolated from a contact child I2 days after the beginning of contact acquired the t± character. However the strain isolated from the same child at I9 days again had the character of an attenuated strain.

A.A. Smorodintsev and co-workers (I959) studied in monkeys changes in neurovirulence of vaccine viruses undergoing numerous passages through the intestinal tract of susceptible children. The results of these investigations showed that at some passage level a slight increase in neurovirulence may be observed, but in further passages through the human intestinal tract neurovirulence is again reduced. Such variations in neurovirulence did not go beyond the characteristics of attenuated strains, and after a series of passages (8 to 9 passages for each of the virus types) the degree of attenuation corresponded to the initial.

It is evident that isolation from a contact child of first t± strain and then again t strain (as we observed) reflects variations in neurovirulence similar to those observed by Smorodintsev and co-workers.

CONCLUSIONS

I. In the process of immunization of people with live poliovirus vaccine establishment and multiplication of vaccine virus in the intestinal tract is a necessary factor.

2. According to our data establishment and multiplication of type I and

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type III vaccine polioviruses in the intestinal tract is observed in 100 per cent of vaccinated and of type II vaccine virus in 90 per cent.

3. In the intestinal tract of nonimmune persons maximum multiplication is reached by type I virus (log $10^{3.6}$ TCD_{50}) at 9 days, type II virus (log $10^{2.5}TCD_{50}$) at 10 days and type III virus (log $10^{3.3}$ TCD_{50}) at 11 days after vaccination. The duration of fecal excretion of type I virus is about 33-37 days (average for 14 persons), of type II is over 47 days (average for 7 persons), and type II 39-42 days (average for 12 persons).

4. In the intestinal tract of immune persons type I vaccine virus multiplies for shorter periods (12-15 days) and is excreted in smaller amounts compared to those in non-immunes. We did not observe any difference in susceptibility to type III vaccine virus in the immune and the non-immune.

5. All the three types of vaccine virus may be spread by contact in a community.

6. Prolonged multiplication of type I vaccine virus in the intestinal tract of susceptible children and passages through susceptible persons (by contact) do not alter the t and d characes of the virus which indicates the stability of attenuation in the vaccine strain LSc, 2 ab.

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REFERENCES

I. Chumakov, M.P. - On mass oral immunization of population in the Soviet Union against poliomyelitis with live vaccine from A.B. Sabin's attenuated strains.

2. Chumakov, M.P., Voroshilova, M.K., Vasilyeva, K.A., Bakina, M.N. Dobrova, D.N., Drozdov, S.G., Podsedlovsky, T.S., Kostina, K.A., Shirman, G.A., Yankovitch, O.D., Uspensky, J.S., Ashmarina, E.E. - Problems of Virology, I959, 5, 520.

3. Sabin, A.- J AMA , I956, I62, I589.

4. Sabin, A.- J AMA, I957, I64, I2I6.

5. Koprowski, H., Jervis, G., Norton, T., Proc. Soc. Exp. Biol. Med., I954, 86, 2, 244.

6. Koprowski, H., Norton T., Hummeler, K., Stokes, J., Hurt A., Flack A., Jervis, G., J. AMA, I956, I62, I4, I28I.

7. Horstmann, D., Paul J., Melnick J., Deutsch J., Journ. Exp. Med., I957, I06, I, I59.

8. Lwoff, A., Lwoff, M., C. rend. Acad. Sc., I959, 248, I54, cited in 9 and I0.

9. Sabin, A. in Live poliovirus vaccines, U.S.A., Washington, I959, p. I4.

I0. Benyesh-Melnick, M., Melnick, J., Ibid, p. I79.

II. Vogt, M., Dulbecco R., Wenner H., Virology, I957, 4, I4I.

I2. Hsiung, G., Melnick, J., Journ. Immunol., I958, 80, 282.

I3. Smorodintsev, A.A. et al., Virologic and serologic investigations of live poliovirus vaccine, carried out at Leningrad Institute of Experimental Medicine - presented at the 3rd Scientific Conference of the Institute for poliomyelitis research, May 2, I959, Moscow.

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Table I

Excretion of vaccine viruses in vaccinated children and their contacts *

(age 0 to 3 years)

Type of vaccine virus	Immunity status before vaccination	Vaccinated: number tested	Vaccinated: excreted: virus	Vaccinated: per cent	Contacts: number tested	Contacts: excreted: virus	Contacts: per cent
Type I strain LSc,2ab	Without antibody	33	33	I00.0	9	9	I00.0
	With antibody	I3	I3	I00.0			
	Total	46	46	I00.0	9	9	I00.0
Type II strain P 7I2,Ch,2ab	Without antibody	I0	9	90.0	3	I	33.3
	With antibody	9	6	66.7	I	0	0.0
	Total	I9	I5	78.9	4	I	25.0
Type III strain Leon,I2a$_I$b	Without antibody	22	22	I00.0	I	I	I00.0
	With antibody	I2	I2	I00.0			
	Total	34	34	I00.0	I	I	I00.0

* A child was considered an excretor if a virus of the corresponding type could be isolated from one or several stool specimens collected for 4-5 weeks after each feeding.

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Table 2

Excretion of type I vaccine virus by immune and non-immune children

Groups	Number tested	Number of children excreting the virus up to the indicated day *								Average duration of excretion (days)	Incidence of virus isolation (number of positive specimens per each negative)**
		2	6	9	I2	I5	I9	26	29	33		
Children without type I poliovirus antibody	I6	0	0	I	0	2	I	5	5	2	25	3.50:I
		0.0	0.0	6.3	0.0	I2.5	6.3	3I.2	3i.2	I2.5		
Children possessing type I poliovirus antibody	7	0	3	2	2						8.5	0.78:I
		0.0	42.8	28.6	28.6					93.7%		

* Upper figure - absolute number of children; lower figure - per cent of total number in the corresponding group of children.

** For the period of virus excretion, that is, for children without antibody from 2 to 33 days, for children with antibody from 2 to I2 days.

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Table 3

Results of tests for the t character with strains isolated from vaccinated children and their contacts at various times after vaccination with type I virus

Name of child	Day of virus isolation from the beginning of vaccination or contact	Log TCD_{50}/ ml at 36°C	Log TCD_{50}/ ml at 40°C	t deficit	t coefficient	Strain characteristics
Vil.	2	7.36	$\leqslant$1.36	$\geqslant$6.00	$\geqslant$0.90	t
(vaccinated)	I5	7.36	$\leqslant$1.36	$\geqslant$6.00	$\geqslant$0.90	t
Bur.	2	7.47	0.00	7.47	I.II	t
(vaccinated)	26	7.20	$\leqslant$1.36	$\geqslant$5.84	$\geqslant$0.87	t
Krj.	6	7.03	$\leqslant$1.70	$\geqslant$5.33	$\geqslant$0.80	t
(vaccinated	I9	8.03	$\leqslant$2.87	$\geqslant$5.16	$\geqslant$0.77	t
Aal.	I2	7.36	3.47	3.89	0.58	t$^{\pm}$
(contact)	I9	7.20	$\leqslant$1.36	$\geqslant$5.84	$\geqslant$0.87	t
Reference strain ISc, 2 ab		6.70	0.00	6.70	I.00	t

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Table 4

Results of tests for the d character with strain isolated from vaccinated children at various times after vaccination with type I virus

Name of Child	Day of virus isolation after vaccination	Log PEU / ml at I.I% $NaHCO_3$	Log PEU / ml at 4.4% $NaHCO_3$	d deficit	d coefficient	Strain characteristics
Vil	2	0.00	6.30	6.30	I.70	d
	I5	$\leq$ 2.70	6.88	$\geq$4.I8	$\geq$I.I3	d
Bur.	2	0.00	7.30	7.30	I.97	d
	26	$\leq$ 2.70	7.29	$\geq$4.59	$\geq$I.24	d
Reference strain LSc, 2 ab		0.00	3.70+	3.70	I.00	d

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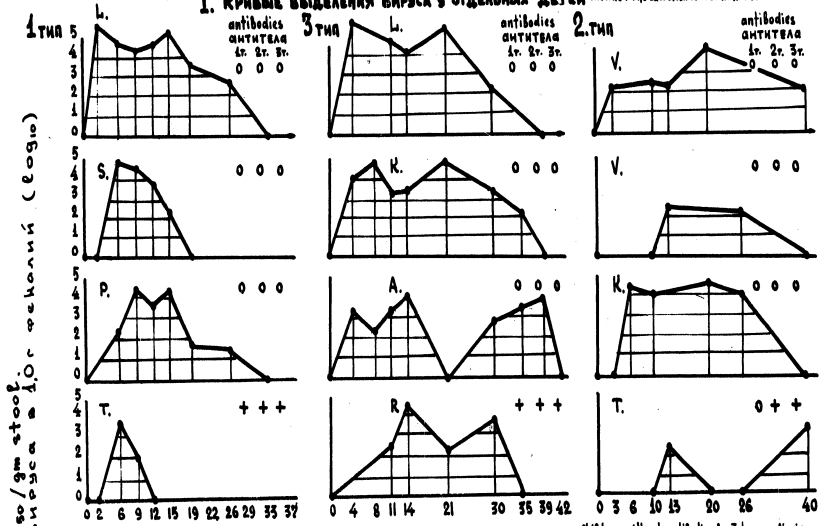
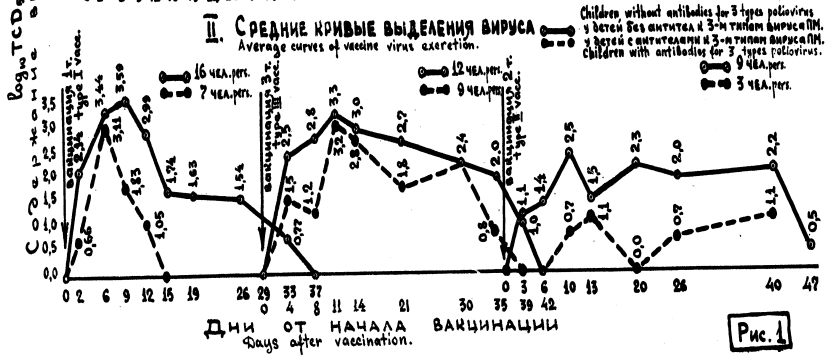
Dynamics of poliomyelitis vaccine virus exeretion Fig. 1.

Динамика выделения вакцинного вируса полиомиелита

I. Кривые выделения вируса у отдельных детей Vaccine virus exeretion curves in individual children.



II. Средние кривые выделения вируса Average curves of vaccine virus exeretion.



Log TCD50/gm stool. Среднее количество вируса в 1,0 г фекалий (Log10)

Дни от начала вакцинации
Days after vaccination.

Рис. 1

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Динамика выделения вакцинного вируса полиомиелита I типа у детей, контактировавших с привитыми

Dynamics of type I poliomyelitis vaccine virus excretion in children, who were in contact with vaccinated. Fig. 2.

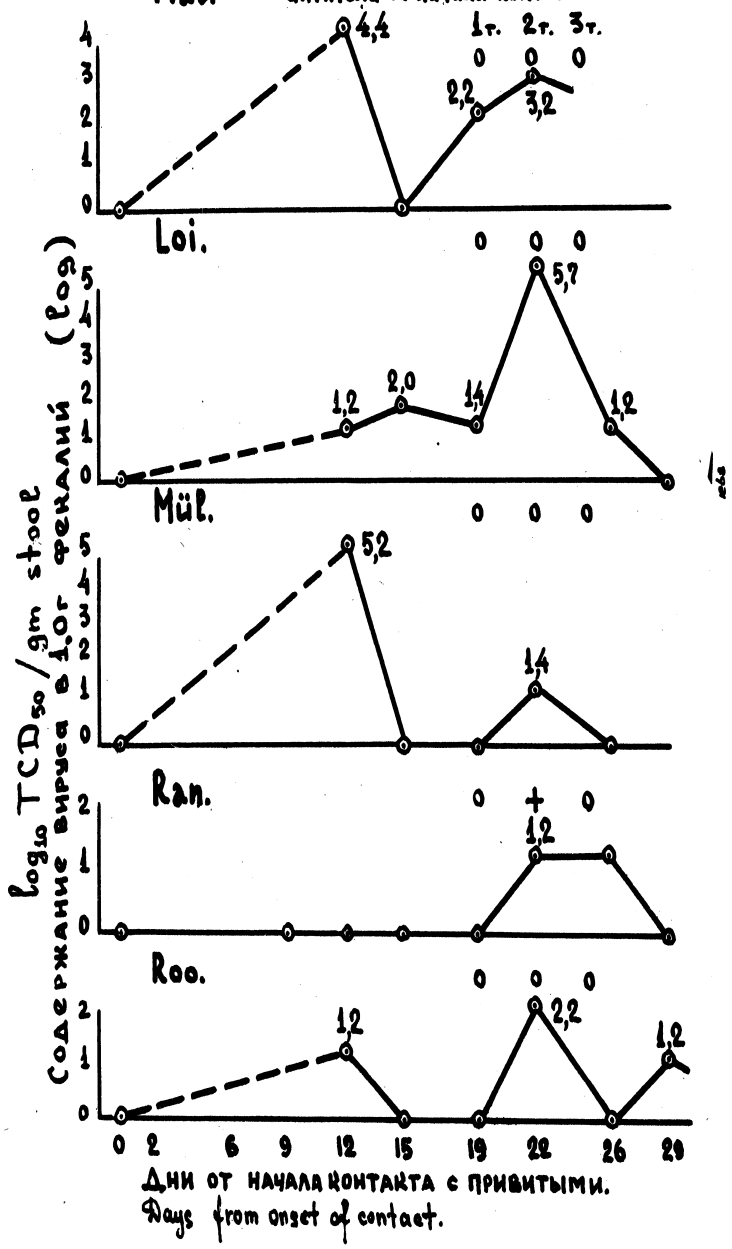

Рис. 2.

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Динамика выделения вакцинного вируса полиомиелита II типа у ребенка, контактировавшего с привитыми

Dynamics of type II poliomyelitis vaccine virus excretion in a child, who was in contact in vaccinated. Fig. 3

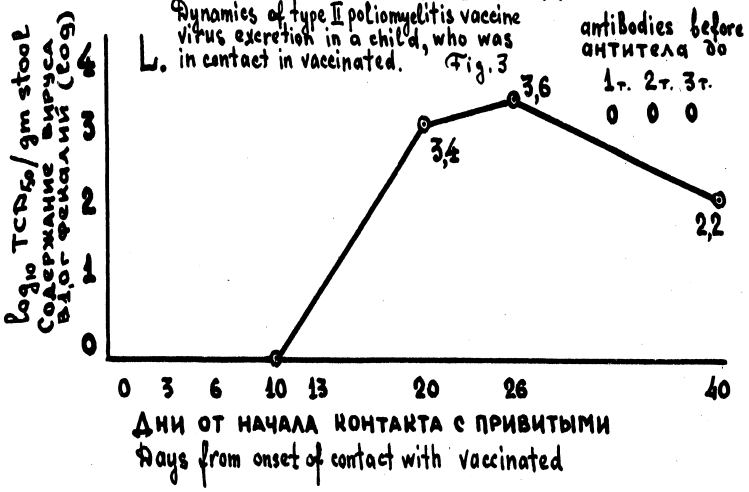

Рис. 3.

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Динамика выделения вируса I т. у вакцинированных и контактных детей

Dynamics of type I virus excretion in vaccinated and contact children. Fig 4.

Штриховкой показаны пробы, вирус из которых исследовался на t и d признаки
Shaded columns represent stool samples examined for t and d markers

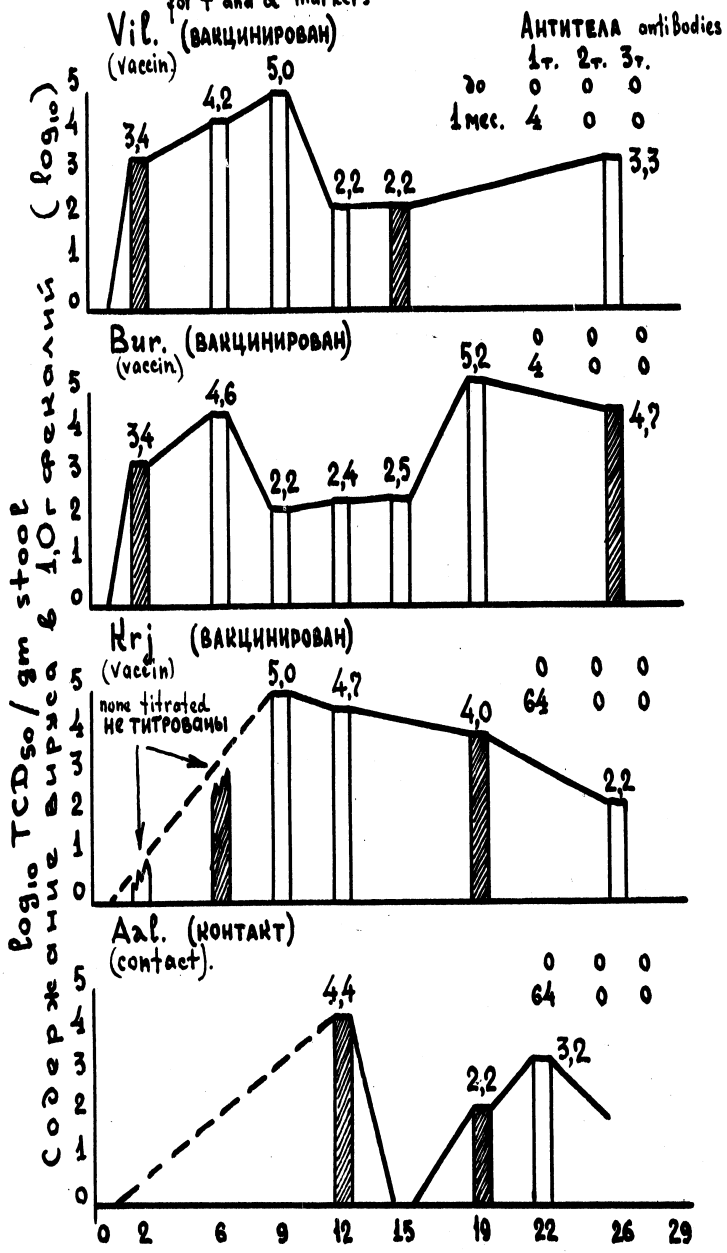

Рис. 4.

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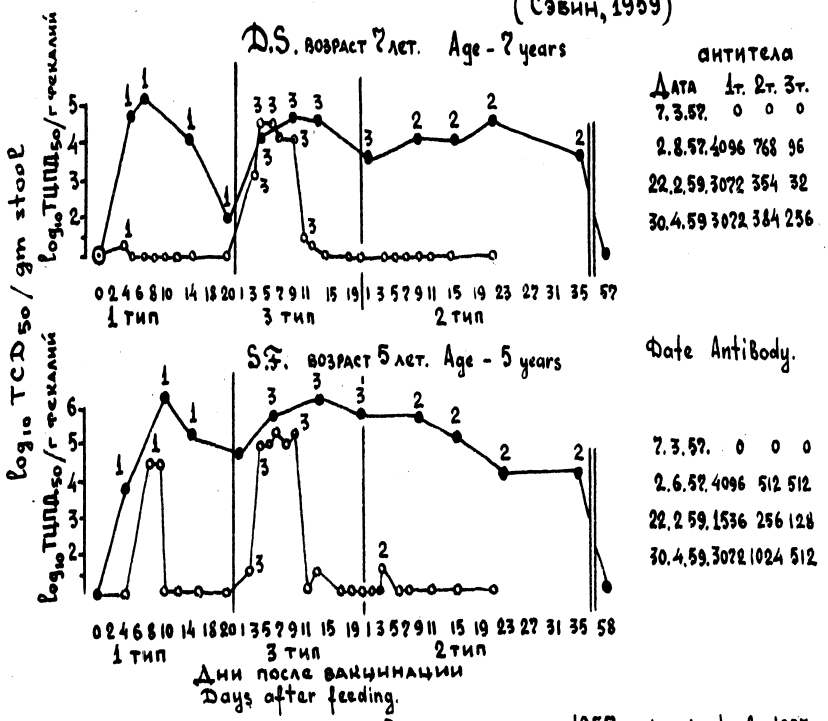
Размножение вируса у трижды негативных детей после первого скармливания 3 типов полиовирусной вакцины с 3-х недельным интервалом и последующего скармливания через 2 года (Сэбин, 1959)



антитела

Дата	1т.	2т.	3т.
7.3.57.	0	0	0
2.8.57.	4096	768	96
22.2.59.	3072	384	32
30.4.59	3072	384	256

Date Antibody.

7.3.57.	0	0	0
2.6.57.	4096	512	512
22.2 59.	1536	256	128
30.4.59.	3072	1024	512

●—● Вирус в фекалиях 1957г. virus in stools 1957.
○—○ —"— —"— 1959г. virus in stools 1959.

Virus multiplication in triple negative children after initial feeding of 3 types of poliovirus vaccine strains at 3-week intervals and after refeeding in same manner 2 years later. (Sabin, 1959.) Fig. 5.

Рис. 5.

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STAT

FEATURES PECULIAR TO THE MULTIPLICATION OF VACCINAL STRAINS OF THE POLIOMYELITIS VIRUS IN THE INTESTINAL CANAL OF CHILDREN DURING THE PRIMARY AND REPEATED IMMUNIZATIONS

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L.M.Kurnosova, A.A. Smorodintsev.

The Department of Virusology of the AMS of the USSR Institute of Experimental Medicine

/ received on 26.III.1960./

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1. As an important indicator of the activity peculiar to the living attenuated vaccine against poliomyelitis serve the intensity and reproduction time of vaccinal strains of the virus in the intestines of the inoculated humans. These two factors are contributive to the creation of a general and local immunity protecting the vaccinated from the disease in case of infection with pathogenic strains of poliomyelitis viruses.

2. The quantitative dynamics characteristic of the poliomyelitis virus reproduction in the childrens' intestines, when these are vaccinated with an attenuated culture, is featured by the appearance of the virus in the first days upon vaccination, rapidly rising titre by the 4-7-th days, no reduction in the number of viruses until the 21-28 days with subsequent gradual elimination of the viruses from the intestine by the 30-50-th days.

3. All of the 3 types of the virus propagate in the intestines of the vaccinated children with fairly high intensity, whereby the virus of the I type seems to make the best showing.

4. A diminuition in the dosage of the virus introduced down to 10.000 TCD_{50} and below this level tends to progressively lower the activity of the vaccinal infection in the intestinal canal.

5. The experience has shown that there are definite correlations between the intensity of virus multiplication in the intestine and the extent to which is rising the antibody titre in the blood of the vaccinated child.

In children whose blood prior to the administration of vaccinal strains, had virus=neutralizing antibodies - a less marked propagation or its total absence could be noted.

In 50 -60% of children with antibodies in their blood - multiplication of vaccinal strains in the intestine is either lacking completely, or the virus can be revealed in the intesti-

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nal contents for a very short time only.

7. The propagation of the vaccinal virus strains in the intestinal canal of inoculated children tends to stimulate a regular accumulation in their blood of virus=neutralizing antibodies and a development of local insusceptivity of the intestinal tract, which manifests itself no less intensively than in children with a naturally developing immunity.

8. Most of the children inoculated with the live vaccine become completely immune to massive doses of repeatedly administered vaccinal poliomyelitis virus of the same type.

9. When vaccinating one half or one third of all children in the age group 1-3 years from among those looked after in closed establishments there occurs a gradual infection of the non=vaccinated ones / contact subjects/ with vaccinal viruses belonging to all the three types, which in the space of 3-4 months - covers 50-80% of all children. The intensity of the virus dissemination by the vaccinated children depends upon their age and the conditions characterizing their contacts with thenon-vaccinated subjects.

10. The indices characteristic of the virus content in the fecal matter of the contacted children are somewhat lower than those found in vaccinated subjects and vary from 10^1 to 10^5 TCD_{50} per 1 gram of the fecal matter. The time intervals for the elimination of the viruses fluctuate from 10 to 60 days / on the average-30 days/. The maximal number of contact infections developed on the 30-40-th days after introduction of the virus into a closed establishment for children of the creche type.

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11. The blood of contacted or vaccinated children showed a rising titre of virus=neutralizing antibldies with clearly distinguishable correlations between the data of the virusological and serological investigations.

12. An intensive infection of non=vaccinated children finding themselves in contact with inoculated subjects is observed only under conditions typical for a primitive and protracted contact which is peculiar to the children of the creche age. In the instance of senior age groups contact infections with vaccinal virus strains are rather accidental and bear no epidemiological importance.

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STAT

CHANGED VIRULENCE FOR MONKEYS OF ATTENUATED SABIN STRAINS FOLLOWING THEIR PROLONGED PASSAGES THROUGH THE INTESTINAL TRACT OF SUSCEPTIBLE CHILDREN

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1. Prolonged passages of attenuated A.Sabin vaccinal strains of the types I,II and III via the intestinal tract of susceptible children are not condicuve to a greater intensification of neurovirulent properties than actually observed in examinations of children at various dates after single vaccination.

With repeated introduction to children of attenuated virus strains endowed with higher neurovirulence one can usually observe apathogenous virus variants excreted from the intestines.

2. Prolonged passages of vaccinal strains via the intestinal canal do not stimulate continuous rise of their neurotropic activity, but are attended by the appearance of variants distinguished from the initial strains by the intensified intraspinal virulence for monkeys / paralizin dose/ 1.0-3.0 above the normal.

3. Analogous results were obtained following examination of neurovirulent properties of the poliomyelitis virus strains isolated from children at various dates after their contact with vaccinated subjects.

4. The data of histopathological examination of the spinal cord makes it certain that thepassage strains under examination fairly regularly attain the lumbar enlargment. This confirms the authentity of the basic data underlying this work, which rest upon the quantitative characteristics of neurotropic activity of the passaged viruses, ascertained by the method of monkey infection by the intraspinal route.

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5. To feature morphological changes in the lumbar enlargment of monkeys infected into the 4th intervertebral space microscopic inspection of 20 blocks was made, effected at a distance of 1 mm from each other, to reveal portions with cicatrisation. This sign served as a criterion for the evaluation of the results of the intraspinal titration, and the monkeys showing no cicatrix were excluded from the experiment.

6. The studied passaged strains introduced into the lumbar enlargment not infrequently gave rise to motor disturbances, these having been noted in approximately 25% of the monkeys infected with the passaged viruses. The intensity of motor disturbances differed in individual instances and showed no definite regularity in diverse passages.

7. In a selective histological examination of infected monkeys considerable changes of poliomyelitic nature were disclosed in the spinal cord of animals with paralysis or paresis of the motor muscles.

8. Viewed morphologically the central nervous system of diseased monkeys becomes the site of affected and destroyed nervous fibers, predominantly in the region of the anterior horns of the spinal cord, There is also an acute inflammatory reaction, which spreads along the entire central nervous system.

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The determination of the dosage of vaccine for the type I /CHAT/ and the type III /Fox/

H. Dobrowolska

From Virology Department of the State Institute of Hygiene, Warsaw

Preliminary Communication

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In connection with the preparation of the vaccination campaign in Poland, studies were inaugurated regarding the immunising properties of the vaccine, depending on the dose introduced inzo the organism.

The investigation was conducted in a Home for Children. 37 children aged 6 months to 3 years were taken into account. The examination of the specimens of stool and blood were carried out before the administration of the vaccine. Then, the living attenuated strains of Koprowski type 1 /CHAT/ have been administered orally; the following dosage was used - 1 ooo ooo, 2oo ooo and loo ooo $TCID_{50}$. Subsequently specimens of stool were collected from the vaccinated children after a 3, 7 and 30 days. Specimens of blood were also collected again after 30 days.

At the same time i.e. 30 days after the first vaccination /type 1 CHAT/ a second dose of the living attenuated Koprowski strein type 3 /FOX/ was given to the same children. The dosage amounted to 2oo ooo and loo ooo $TCID_{50}$. The second vaccination was followed by the collection of specimens of stool 3 and 7 days after administration of type 3 vaccine. Blood was also examined for a second time after 3o days. The last blood control test was performed 3 1/2 months after the administration of the type 1 virus.

The results of the sirusological examinations are given in the table Nr 1.

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Table Nr 1

Out of the 37 children examined before vaccination presence of the Polio virus type 1 in stool was ascertained in 4 cases. However, prior to vaccination no antibodies against the virus Polio type 1 have been detected in the above named cases. One might suppose that we had to deal with a fresh, symptomless infection, and that the antibodies have not been produced, as yet.

The table indicates that the highest percentage of isolated virus strains was obtained with the dosage 1 ooo ooo $TCID_{50}$. on the other hand a lower percentage was obtained when the dosage amounted to 2oo ooo, finally the lowest one after the application of loo ooo doses.

In general, irrespectivelly of the dosage, the virus type 1 has been isolated in 80%. It should be added that in 2 cases neither the isolation of the virus nor the increase of antibodies could be demonstrated.

In a certain number of cases the virus type 1 was isolated after 30 days.

The results obtained after the vaccination with the virus type 3 are similar to those arrived at with the virus type 1. In all, the virus has been isolated in 76%.

It should be indicated that the isolation of the virus was attempted 3 and 7 days after vaccination, if the period of study should be lenghtened the percentage of positive findings would probably be much higher.

As a result of our investigations we could ascertain that the viruses used for vaccination, have definite affinity to

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the intestinal tract, and can multiply there. The vaccine administered to children - in the dosage, named above, - produced no symptoms of the disease.

Serological examinations performed prior to vaccination, indicated that with the exception of three children, no child in the group had antibodies against the 3 types of the Polio virus.

The antibodies concentration in 2 children amounted to 1/8 for the types 1 and 3, and that for the type 2 to 1/4. In the third child the concentration of antibodies for the type 1 only, was 1/8.

The results of the blood examination following vaccination are given in the table Nr 2.

Table Nr 2

The table shows that the antibodies against type 1 showed the highest increase after 110 days. No antibodies have been detected in 16% of children, i.e. that in 84% the presence of antibodies has been proved, and antibodies in the concentration from 1/16 to 1/1024 appeared in 72% of children.

It should be added, that the level of antibodies showed variations, and even a decrease after 30 and 60 days.

The highest percentage of positive results was obtained for type 3 after 80 days. This percentage comes to the 100% concentration from 1/64 to 1/2048.

In discussing this tabel attention should be called to the fact, that the dosage of the vaccine administered to the children was not the same in all the cases, and at loo ooo $TCID_{50}$,

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has not produced antibodies in 2 children, and the virus failed to develop in their intestines.

In follows from our experiments that the vaccine prepared with the Koprowski strains has fully established its immunogenic properties.

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Table Nr 1

Excretion of CHAT and Fox viruses by individuals viruses

Different doses

The vaccine dose $TCID_{50}$	Number of chil examined	Stool collected I before vaccination	II	III	IV	V after feeding type 3 /Fox/	IV
1 000 000	12	3/12 type 1	11/12	11/12	4/11 type 1		
200 000	11	0/11 type 1	7/11	9/11	3/8 type 1	12/15	1/7 9/16 type 1
100 000	14	0/14 type 1	7/14	9/13	2/13 type 1	11/11 8/11 type 1 type 3	7/11 type 3
T o t a l		3/57	25/37	29/36	9/32	20/26	6/27
		8,1%	67%	80%	28%	76%	59%

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Table Nr 2

The development of antibodies after vaccination with the attenuated Polio vaccine type 1 and type 3

Type	Day of examination	Serum dilution					
		0	4-8	16-32	64-128	256-512	512
1	30	7/33 21%	3/33	14/33	5/33	4/33	0/33
1	60	7/24 29%	6/24	4/24	3/24	0/24	4/24
1	100	4/25 16%	3/25 12%	3/25 . 12%	3/25 12%	6/25 24%	6/25 24%
		16%	12%		24%		48%
3	30	3/24	2/24	3/24	7/24	6/24	3/24
3	80	0/25 0%	0/25	0/25	3/25	6/25	16/25
						100%	

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STAT

The Antibody Response in Children Vaccinated with a) the Live Actenuated Polioviruses and b) the Fourth Dose of Inactivated Poliovaccine

Karel Žáček, Vladimír Vonka and Ervín Adam

From the Virus Department of Institute of Sera and Vaccines and from the Clinical Laboratory for Poliomyelitis Research, Prague

The different aspects of the safety and effectiveness of immunization by the inactivated vaccine and recently also by the live poliovirus vaccine have been discussed in some of our previous papers (1,2,3). In this study we present some results concerning the investigation of antibody response in children vaccinated in the field trial with live

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attenuated polioviruses, undertaken in Czechoslovakia in 1958/59, and children who received the fourth dose of the Salk vaccine in 1959.

Material.

The mass vaccination of children with the inactivated poliovaccine of Canadian origin started in Czechoslovakia in May 1957. Two doses containing 0.2 to 0.3 ml of this vaccine were administered intradermally in two four week intervals to a total of 2.25 million of children aged 1 to 7 years, partly also up to 14 years of age. In the spring of 1958, i.e. about 7 to 8 months after the primary immunization, these children received the third dose of the inactivated vaccine in the amount of 0.2 to 0.3 ml intradermally.

In 1958/59 a field trial with the live poliovirus vaccine was carried out in Czechoslovakia. In this trial a total of about 140,000 children who had been previously vaccinated with three doses of Salk vaccine, were immunized by the three types of attenuated live polioviruses (Sabin) in four regions of Czechoslovakia.

The study material consists of two groups:

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Group A (live poliovirus vaccine) is represented by 93 (82 and 88, respectively) of children aged 2 to 8 years, who received three doses of Salk vaccine in 1957 and 1958 and in the course of the field trial were fed with live attenuated polioviruses (type 1 in December 1958, type 3 in January 1959 and type 2 in February 1959). Children were selected at random with approximately the same number of children in individual age groups.

Blood samples were taken in November 1958, i.e. about 7 to 8 months after third injection of Salk vaccine (approximately 1 month before the administration of type 1 virus) and second blood samples were drown in March 1959, i.e. approximately one month after feeding with the last type 2 of virus.

Group B (the fourth dose of Salk vaccine) is represented by 159 (282 resp.) of children aged 2 to 10 years who received three intradermal injections of Salk vaccine in 1957 and 1958 and the fourth dose of the killed vaccine given in the amount of 1 ml subcutaneously in May 1959.

The first blood samples in this group were taken simultaneously with the administration of the fourth dose of

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Salk vaccine and the second blood samples were taken 14 days after the injection.

Methods

The paired serum specimens were kept frozen and neutralizing antibodies to three types of polioviruses were tested simultaneously by pH test in plastic panels and by CPE test in tube tissue cultures from monkey kidney cells. Both tests were carried out by the conventional method with 100 TCD_{50} of virus and 1 hour incubation of the virus—serum mixture at room temperature. The sera were quantitatively assayed in five fourfold dilutions from 1/4 to 1/1024.

Results

Table 1 shows the results of the investigation of paired serum specimens ontained from children aged 2 to 8 years fed with the live polioviruses in the regions of Ústí and Jihlava, and the analogic results of the investigation of paired serum specimens obtained from children aged 2 to 10 years vaccinated with the fourth dose of Salk vaccine.

From the table it can be seen that children without homologous antibodies prior to vaccination responded to the live polioviruses with a significant rise of antibodies to

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type 1 in 95%, type 2 in 93% and to type 3 in 94 per cent of vaccinated children.

The rise of antibodies to type 1 was found in 50%, to type 2 in 67% and to type 3 even in 83 per cent of children without homologous antibodies, who received the fourth dose of Salk vaccine.

In contrary to the better antibody response of the homologically negative children to the vaccination with live polioviruses especially to type 1 and 2, the antibody response of children possessing previous homologous seroimmunity in both groups is approximately the same and in some instances the response to the killed vaccine was higher than to the live poliovirus vaccine.

A more detailed quantitative analysis of these results is presented in table 2.

This table shows that after the vaccination with live polioviruses homologically non-immune children developped low titers of type 1 antibodies in 32%, and high titers in 68% of the children tested. In type 2 high levels of antibodies were found in 85% of the children and the weakest response was found to type 3, to which type the low titers of antibodies were found in 56% and high levels of anti-

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bodies only in 44% of the children fed.

On the left side of the table 2 there are presented the results of the investigation of children vaccinated with the fourth dose of Salk vaccine. From these results it can be seen that in homologically non-immune children the antibody response to type 1 was very week in 90% of the children, low levels of type 2 and 3 antibodies were found in 36 and 61 per cent, respectively.

These results, especially the surprisingly good response to type 3 and to a certain extent to type 1, too, obtained in children vaccinated with the fourth dose of Salk vaccine, let us to further analysis made in view of the fact that this effect could be caused by:

a) pre-existing immunity to type 2, which could induce the heterotypic formation of type 1 and 3 antibodies,

b) the presence of very low levels of homologous antibodies in the pre-immunization serum samples, which could not be detected by the conventional tests used,

c) antigenic potency of the vaccines used.

The influence of pre-existing immunity to type 2 on the antibody response to type 1 and 3 can be observed in the results presented in tables 3 and 4.

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Table 3 shows the results of the investigation of 282 children vaccinated with the fourth dose of Salk vaccine. These 282 children include first group of 159 of children selected at random plus one other group of 123 of children all aged 7 and 8 years, which were subcutaneously vaccinated in the same time as the first group in schools.

From these 282 of children, 107 had no type 1 antibodies and 114 of individuals were without type 3 antibodies prior to vaccination. From the 107 of children without type 1 antibodies 30 possessed type 2 antibodies and 27 lacked this type of antibodies in the pre-vaccination serum specimens. Out of these 27 of children lacking type 2 antibodies prior the booster injection, 85% did not develop type 1 antibodies at all, while 15% of children attained only very low levels of type 1 antibodies and in none of these children type 1 antibodies in titers of 1/64 or higher were demonstrated 14 days after the administration of the fourth dose of Salk vaccine.

A similar situation was also found in type 3; good antibody response to this type was found in a relatively high percentage of children who had possessed antibodies to type 2 prior to the booster injection and this percentage was even considerably higher in type 3 than type 1. The results of the investigation of type 3 antibody response in

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children who had no type 2 antibodies prior to the fourth injection, proved to be very interesting. Out of these 22 children 32% did not respond to the booster dose at all, while remaining 68% developed antibodies to very low titers, again in no one case reaching the titer of 1/64 or higher.

In the table 4 there are compared the similarly arranged results obtained in children, who were fed with live attenuated polioviruses. As expected, it was impossible to prove the dependence of type 1 and 3 antibody response upon the state of previous type 2 seroimmunity: rather the contrary was right: a higher type 3 antibody response was observed in children, who had no type 2 antibodies prior to the vaccination.

With respect to the clearly ascertained dependency of type 1 and 3 antibody response upin the previous state of immunity against type 2 in children vaccinated by the Salk vaccine, we compared the antibody response to the booster injection of Salk vaccine and to the live virus vaccine in children lacking antibodies to any type of polioviruses (triple negative children) /Table 5/.

From the table 5 it can be seen that after the fourth

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dose of Salk vaccine 19 out of 22 triple negative children did not respond to type 1 and remaining 3 children developed type antibodies only in titers of 1/4. To type 3 six children remained negative, 10 children developed very low titers of 1/4 and the remaining 6 children low titers of 1/16. Only in type 2 a relatively good immunization effect of a single dose of the killed vaccine was observed in triple negative children: only 4 children remained negative, 7 children developed low titers, while in 11 individuals a relatively high antibody response was noted.

In contrast to these results, the analogically arranged results of the investigation of 11, resp. 10 of triple negative children, fed with live attenuated polioviruses, show that all these children responded to type 1 and 3, with only one child remaining negative against type 2 of virus (which was administered as the last).

An attempt to detect the very low levels of type 1 antibodies which could not be demonstrated by means of conventional tests used, and which nevertheless could be present in the prevaccination serum specimens and influence the homologous antibody response to the booster injection of killed vaccine, is briefly described in table 6.

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In this experiment 14 out of the 48 of sera previously negative in the routine pH and CPE tests inhibited the cytopathogenic changes in CPE test performed with 10 TCD_{50} of type 1 virus and 6 hour incubation of the virus-undiluted serum mixture. From the results of this experiment it can be drown that from individuals who had a very small quantity of type 1 antibodies (specific ?) in the pre-vaccination serum specimens, responded to the booster injection more children than from those who were without any trace of antibody in repeated more sensitive test. On the other hand, however, almost all the children who in both group developed type 1 antibodies after the booster injection had possessed type 2 antibodies prior the vaccination.

Discussions and Conclusions

The degree and duration of the effect produced by three injections of inactivated trivalent poliovaccine was studied extensively in a great number of vaccinated children. Salk and many other (4,5,6,7) assume that the response of an individual to three doses of killed vaccine given at properly spaced time intervals depend mostly on

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the amount of antigen administered.

When using his own reference vaccine Salk (4,5) was able to demonstrate in triple negative children a relatively very good antibody response with a high order of persistence.

Salk suggests further that the failure of response can be either the result of an inadequate or impotent antigenic stimulus or, in some individuals because of a relatively poor antibody responding mechanism.

When considering the response to booster injections Salk (4) supposes that the antibody level induced is influenced not only by the amount of antigen contained in the booster injection but, in the first place, by the quantity of antigen applied at the time of primary vaccination, and that the persistence of antibodies developed following the primary immunization or by booster injections is influenced in a similar way.

Salk paid a special attention (5) to the quantitative relations between the amount of antigen administered and the degree of antibody response after the primary vaccination as well as after the booster stimulus.

He found a very good antibody response to all types of

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polioviruses in individuals after primary vaccination with two doses containing 2 ml and 1 ml of vaccine, respectively. The response of individuals vaccinated with two doses containing 0.5 and 0.25 ml, respectively, to the booster injection administered one year later was relatively very good, too.

A somewhat lower antibody response to booster injection was demonstrated in persons primarily vaccinated with two doses containing 0.125 and 0.0625 of vaccine; nevertheless even in this group no one child was found without antibody response and the mean titer of type 1 antibodies after the booster injection was about 1/64. The weekest response to the booster dose (with decline to non-detectable levels) was most evident for type 1, in the case of the group of children who received the smallest dose of reference vaccine; the most effective response and the most durable could be recorded for the type 2 component of the vaccine.

When studying the results achieved with the reference vaccine and those reached with commercial vaccines, Salk found that the commercial vaccines tested more closely comparable in performance to the larger doses of reference

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vaccines than to the smaller doses.

In connection with our own results we will pay attention especially to the effect of the fourth dose of Salk vaccine in children who received three injections of killed vaccine, in whom however, no pH antibodies to one or more types of polioviruses could not be demonstrated. As mentioned above, these children received the fourth dose approximately one year after the third one which was administered about 7 to 8 months after the primary immunization with two doses of killed vaccine given in 0.2 to 0.3 amounts intradermally.

We point out that this quantity of vaccine used by us to the primary immunization is higher than the amount of antigen given by Salk in one group of children investigated (0.0625 ml). When we are trying to evaluate we shall compare them especially with those achieved by Salk with the smallest amount of vaccine.

C o n c l u s i o n s

1) In 378 of children aged 2 to 10 years no type 1 antibodies could be demonstrated by means of the pH test in about 38% of children 8 to 12 months following the third

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dose (0.2 to 0.3 ml intradermally) of the inactivated polio-vaccine and approximately 19 months after the primary immunization with two intradermal injections containing 0.2 to 0.3 ml of Salk vaccine; in 13 to 19% of these children no type 2 antibodies were present and about 40% of them did not possess any antibodies against type 3 poliovirus.

2) In these sensitised but prior the administration of the fourth dose of Salk vaccine "homologously non-immune" children, a single subcutaneous booster injection of 1 ml of killed vaccine resulted in a significant rise of type 1 antibody in 50% of the vaccinated individuals while the rise of type 2 and 3 antibodies amounted to 67% and 83% of children, respectively.

3) Nevertheless, a more detailed analysis of this surprisingly good effect of booster injection, especially when type 3 antibody is considered, in children without homologous immunity revealed that a remarkable antibody response to types 1 and 3 appeared mostly in individuals possessing type 2 antibodies prior the administration of the fourth dose of Salk vaccine.

On the other hand, 85% of children lacking type 2

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antibodies prior the booster injection developed no type 1 antibodies at all, while in the rest of them only very low antibody response was observed, reaching not more then the titer of 1/32.

A similar situation was observed in type 3 antibody response; 32% of children lacking type 2 antibodies developed no type 3 abtibodies at all, and in the remaining 68% of children very low titers were determined reaching the maximum of 1/32.

4) These results are in a good accordance with those achieved in triple negative children. In the first group of children lacking both the homologous and type 2 antibodies, as well as in the group of triple negative children, only a very week response could be recorded, following the booster injection, in type 3 antibodies, and almost negligible or rather negative response in type 1 and only type 2 antibody response was relatively good.

Comparing our results achieved after the fourth dose of Salk vaccine in children who previously received three intradermal injections of the inactivated poliovaccine with those attained in similar study by Salk, a considerable quantitative difference can be recorded. The seemingly

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good effect of the fourth dose of poliovaccine, particularly in type 3, noted in our homologously negative children should be in fact rather considered as a heterotypic antibody response in individuals having antibodies against type 2 poliovirus prior the booster injection.

In agreement with Salk's conception we may presume that the immunization effect in our children vaccinated with three doses of killed vaccine was very week. The booster effect achieved by Salk, however, was relatively much better in children primarily immunized with two doses of 0.125 ml of inactivated poliovaccine, in spite of the fact that our primary immunization was carried out with greated quantity of vaccine which was moreover applied intradermally, i.e. by the technique which is known to produce a better immunizing effect than the same amount of antigen injected by subcutaneous or intramuscular routes.

As concerning the antibody persistence, we assume that the low antibody levels following the booster injection will persist only for a short period, may be no longer than a few weeks. This concerns mainly the low type 1 and type 3 antibody titers developing especially in individuals lacking homologous and type 2 antibodies prior to the booster injection.

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With the exception of type 2 we were not able to demonstrate in our material a good effect of the fourth injection of the killed poliovaccine in children sensitized with three doses of inactivated vaccine, particularly in those without homologous and type 2 antibodies prior the booster injection.

In our children aged 2 to 10 years immunized in 1957 and 1958 with three doses of the Salk vaccine a high percentage of individuals lacking type 1 or type 3 pH antibodies was found about 1 year after the third dose, moreover in a relatively high proportion of them no type 2 antibodies were present; this is why we do not think that the fourth dose or further doses applied once a year would induce sufficient booster effect which could provide an effective and durable immunity of the individuals mostly exposed to infection.

We think rather that in children in whom no good seroimmunity developed following the primary immunization from various reasons, further doses of vaccine applied at long intervals do not represent the booster effect, but more likely the beginning of a new primary immunization process. Because one dose of killed vaccine is obviously not suffi-

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cient for this primary immunization, we can formulate our answer to the question of how many injections of inactivated poliovaccine are necessary for providing an effective and durable individual immunity by these words: when vaccines of low potency are used (as is the case of most commercial products) we believe that it would be necessary to immunize with two successive doses applied in a short interval given prior the beginning of every new epidemic season.

For the present time it is difficult to say how often this cycle should be repeated in practice but we are rather of the opinion that it should be repeated until the susceptible individuals partially protected by the Salk vaccine will be solidely immunized by the natural infection or the better degree of protection will be achieved by vaccination with live attenuated polioviruses.

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References

1. Žáček, K., et all.: Journal of Hygiene, Epidemiology, Microbiology and Immunology (Czechoslovakia), III/1: 60-66, 1959.

2. Škovránek, V., et all.: Ibid, 11/4: 469-477, 1958.

3. Škovránek, V., Žácek, K., et all.: Paper Presented on the Conference on Live Poliovirus Vaccine, Washington, June, 1959.

4. Salk, J.E., J.A.M.A. 167: 1-7, 1958.

5. Salk, J.E., J.A.M.A. 158: 1239-1248, 1955.

6. Salk, J.E., J.A.M.A. 162: 1451-1459, 1956.

7. Beswick, T.S.L., Paper Presented on the 6th Symposium of European Association against Poliomyelitis, Munich, 1959.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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Table 1

4th Dosis of Salk Vaccine /Plzen/

Type	Number of children investigated	Antibody status prior vaccination /pH test/	Number	Significant rise in antibody +)	
				N°	per cent
1	159 /39% neg./	Negative	62	31	50
		4 - 32	36	29	80
		64 - 512	61	36	58
2	159 /13% neg./	Negative	21	14	67
		4 - 32	81	67	83
		64 - 512	57	32	56
	/41% neg./	Negative	65	54	83
		4 - 32	48	34	71
		64 - 512	46	22	48

+) These data are based on:

a) 4x increase in pH and CPE test, or b) 4x increase in CPE test without rise in pH test, or c) 8x increase in pH or CPE test.

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Table 1

Poliomyelitis Antibody Response in 159 children Aged 2-10 years, Vaccinated with the 4th Dose of Salk Vaccine (in the region of Plzen and in 93 /82 and 88 resp./ Children Aged 2-8 Years, Vaccinated with Live Poliovirus Vaccine - Sabin /in the regions of Ústi and Jihlava/.

Live Vaccine - Sabin (Ústí and Jihlava/

Type	Number of children investigated	Antibody status prior vaccination /pH test/	Number	Significant rise in antibody +)	
				N°	per cent
1	93 /39% neg./	Negative	36	34	95
		4 - 32	21	14	67
		64 - 512	36	23	64
2	82 /17% neg./	Negative	14	13	93
		4 - 32	36	30	83
		64- 512	32	21	63
3	88 /39% neg./	Negative	34	32	94
		4-- 32	37	20	74
		64- 512	27	12	44

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Table 2

Antibody Response in Children Lacking Homologous Antibodies Prior Vaccination (Negative Children) to the Fourth Dose of Salk Vaccine and/or to the Live Poliovirus Vaccine (Sabin)

(More Detailed Data from Table 1)

4th Dosis of Salk Vaccine						Live Vaccine - Sabin					
Type	N° of negatives (pH test)	N° of children which developed antibodies after booster injection	Homologous antibody response +) Titre	No	Per cent	Type	N° of negatives (pH test)	No of children which developed antibodies after vaccination	Homologous antibody response +) Titre	No	Per cent
1	62	31 (50% positive)	4- 32 64- 512	28 3	90 10	1	36	34 (95% positive)	4- 32 64 512	11 23	32 68
2	21	14 (64% positive)	4- 32 64- 512	5 9	36 64	2	14	13 (93% positive)	4- 32 64 512	2 11	15 85
3	65	54 (83% positive	4 32	33	61	3	34	32 (94% positive)	4- 32 64- 512	18 14	56 44

+) Those data are based on pH and CPE antibody tests.

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Table 3

Type 1 and 3 Antibody Response in Children to the /4th dose of Salk Vaccine/ in Relation to the Status of Homologous and Type 2 Antibody Prior Vaccination

No of children investigated	Type	Without homologous antibodies prior vaccination (pH.test)	Status of Type 2 antibodies prior vaccination (pH test)	Homologous antibody response: Titre	No	Per cent
282	1	107 /38 % neg./	Positive 80children	Negative	21	26
				4 - 32	50	62
				64 - 512	9	12
			Negative 27children	Negative	23	85
				4 - 32	4	15
				64 - 512	0	0
	3	114 /40 %	Positive 89children	Negative	6	7
				4 - 32	41	46
				64 - 512	42	47
			Negative 25children	Negative	8	32
				4 - 32	17	68
				64 - 512	0	0

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Table 4

Type 1 and 3 Antibody Response in Children to the Live Poliovirus Vaccine (Sabin) in Relation to the Status of Homologous and Type 2 Antibody Prior Vaccination

No of children investigated	Type	Without homologous antibodies prior vaccination (pH test)	Status of Type 2 antibodies prior vaccination (pH test)	Titre	Homologous antibody response No	Per cent
93	1	36 /39% neg./	23 Positive children	Negative	1	
				4 - 32	8	35
				64- 512	14	61
			Negative 13 children	Negative	1	-
				4- - 32	3	23
				64- 512	9	69
88	3	34 /39% neg./	Positive 23 children	Negative	1	-
				4 - 32	14	61
				64 - 512	8	35
			Negative 11 children	Negative	1	-
				4 - 32	3	27
				64 - 512	7	64

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Table 5

Antibody Response in Triple Negative Children Aged 2 - 10 Years Vaccinated with the 4th Dose of Salk Vaccine (1 ml subcutaneously/ and in Triple Negative Children Vaccinated with Approximately 100,000 TCD_{50} of the Live Poliovirus Vaccine (Sabin)

4th Dose of Salk Vaccine								Sabin Vaccine						
No of triple negat. children investigated (pH test)	Antibody response /pH test/ Titer							No of triple negat. children investigated (pH test)	Antibody Response (pH test) Titer					
	Type	Negat.	4	16	64	256	512		Type	Negat.	4	16	64	256	512
22	1	19	3	0	0	0	0	11	1	0	1	3	4	1	2
	2	4	1	6	8	0	3	10	2	1	0	1	1	3	4
	3	6	10	6	0	0	0	10	3	0	2	2	5	0	L

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Table 6

Type 1 Poliomyelitis Antibody Response in Children in Relation to the Very Low Amounts of Type 1 Virus Inhibitors and Status of Type 2 Antibodies Prior Vaccination with the 4th Dose of Salk Vaccine

No of sera negative to type 1 in pH and CP tests with 100 TCD_{50} of virus and 1 hour incubation	Status of type 1 antibodies in CP test with 10 TCD_{50} and 6 hours incubation	Type 1 antibody antibody response to the 4th dose of Salk vaccine	Status of Type 2 antibodies prior the 4th dose of vaccine
48	Positive 14	Positive 10	Positive 9
			Negative 1
		Negative 4	Positive 4
			Negative 0
	Negative 34	Positive 13	Positive 13
			Negative 0
		Negative 21	Positive 9
			Negative 12

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ACADEMY OF MEDICAL SCIENCES OF THE USSR

INSTITUTE FOR POLIOMYELITIS RESEARCH

STAT

Repeated Serological Surveys Performed in the General Population of Czechoslovakia before and after the Vaccination of Children with Inactivated and Live Poliovirus Vaccine

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In 1957 mass vaccination of the children with Salk vaccine was started in Czechoslovakia and in the years 1958/59 a controlled field trial with live poliovaccine was performed. In connection with these campaigns of the fight against paralytic poliomyelitis, a number of virological and epidemiological studies were undertaken in our country, including repeated repeated aerological surveys in general population of some Czech regions.(1 - 9).

In these studies the state of seroimmunity of the population was repeatedly investigated before and after the vaccination with Salk vaccine and before and after the feeding of children with live attenuated polioviruses. The presented paper summarizes some results of these investigations.

M a t e r i a l

Vaccination with Salk vaccine

In May and June 1957, 2, 246, 811 of children in Czechoslovakia wre inoculated with two doses of inactivated trivalent poliovaccine. The majority of the children were aged 1 to 7 years, some of them 8 to 14 years. The vaccination was carried out intradermally, each inoculation containing 0.2 to 0.3 ml of vaccine. In autumn of 1957 the vaccination was further extended mainly in the group of children aged 8 to 14 years. In the spring of 1958 the third dose containing 0.2 to 0.3 ml of vaccine was administered intradermally to the children who had received two injections in spring 1957. For these campaigns Canadian vaccine was used.

The number of children vaccinated with killed vaccine in Czechoslovakia up to June 1958 is given in Table 1.

In one region (Plzen) approximately 58% of the children aged 2 to 15 years formerly inoculated with three doses of Salk vaccine

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were inoculated subcutaneously with the fourth injection of 1 ml of killed poliovaccine of Czechoslovak production.

Vaccination with live poliovirus vaccine

The following four regions in the western part of Czechoslovakia were selected for the vaccination with the live poliovirus vaccine (kindly supplied by Dr. Albert B. Sabin, USA): Usti, Liberec, Jihlava and Ostrava, including two industrial regions (Usti and Ostrava, one mixed (Liberec) and one predominantly rural region (Jihlava). The basic data on the number of inhabitants, density of population and morbidity rate of paralytic poliomyelitis in these four regions are given in Table 2.

Simultaneously in all four regions mentioned children mostly at the age of 2 to 6 (partly up to 8 years), inoculated previously with 3 doses of Salk vaccine received the live poliovirus vaccine in the following time intervals: type 1 in the period of 15-20th December, 1958, type 3 in 12-16th January, 1959, and type 2 in the period of - 13 February, 1959.

The number of children fed with live polioviruses in the individual age groups is presented in Table 3.

The individual types of viruses were administered separately in the amount of approximately 100,000 TCD_{50} in 2 drops of 1/10 diluted original virus suspension on a spoon of syrupus simplex.

Sampling of blood specimens

For serological surveys the blood specimens were taken in the following regions and time intervals:

1. In the region of Jihlava, Usti and the city of Prague in the period between January and March 1957, i.e. before Salk vacci-

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nation.

2. The regions of Jihlava and Usti in November 1958, i.e. approximately 7 to 8 months after the third dose of killed vaccine and one month before starting of live poliovirus vaccination.
3. In the region of Jihlava and Usti in March 1959, i.e. about 1 month after feeding of the last type 2 of live poliovaccine.
4. In the region of Plzen in May 1959, i.e. about 1 month before the administration of the fourth dose of Salk vaccine.

The blood specimens were collected at random from all parts of the regions proportionally to the number of inhabitants and in no instance samples from the same individuals were taken, in November 1958 and March 1959.

Specimens were drawn from subjects of different age, divided into 13 groups. Each group consisted from about 60 or 120 individuals according to the number of annual sets in the group.

The blood specimens were taken mostly from the patients in the first days of their admission to the hospitals, not bleeding subjects suffering from infectious diseases, or those who had in their case-history of an infectious disease of CNS. Where it was not possible to gain sufficient number of blood specimens in the hospitals, the samples were taken in creches, nurseries and schools. From one child community or school, however, never more than from 1/7 of the total number of community members the specimens were collected; this material did not exceed more than 10% of total number of specimens gained.

Methods

The sera were inactivated for 30 minutes at 56°C and after adding 500 to 1,000 units of penicillin and streptomycin per 1 ml

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they were kept frozen until investigation.

Neutralizing antibody estimation

The sera were tested:

a) qualitatively by means of the cytopathogenic (CPE) test carried out in tube tissue cultures from monkey kidney cells with approximately 100 TCD_{50} of virus and 1 hour incubation of the mixture of virus and 1/4 diluted serum at room temperature, and

b) quantitatively in the pH test performed in plastic panels with 100 TCD_{50} of virus and sera diluted in fourfold steps from 1/4 to 1/256, with 1 hour incubation of the virus-serum mixture at room temperature.

The blood specimens collected for survey in 1957 were examined only qualitatively in the CPE test, every serum tested in two tubes against each type of virus; the blood specimens gained in Usti and Jihlava regions in the surveys in 1958 and 1959 were examined qualitatively in CPE test (1 tube for 1 serum) and simultaneously quantitatively in the pH test (1 cup for 1 serum dilution); the survey performed in Plzen region in 1959 was done only quantitatively in pH test.

Results and Conclusions

The results of the qualitative investigations of the incidence of poliomyelitis antibodies found in 1/4 diluted serum specimens in CPE and pH tests, respectively, in 3 repeated surveys carried out in 1957, 1958 and 1959 in the region of Usti are given in Table 4, the analogic results gained in the region of Jihlava are summarized in Table 5.

In the Figures 1, 2 and 3 there are presented the results of

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the investigations of CPE antibodies in three repeated surveys reviewed in the average values of both regions, Usti and Jihlava together.

From the tables and figures it can be seen that, when comparing the results gained in 1957 (sera taken before the mass vaccination with Salk vaccine) and in November 1958 (sera collected about 17 months after administration of 2 doses of killed vaccine and about 8 months after administration of the third injection of Salk vaccine), we could observe a certain increase in type 1 antibodies in the corresponding age groups. Similar increase could not be proved in type 3, while there was found a considerably high rise of type 2 antibodies.

Two main factors could be the cause of the increased seroimmunity to type 2 and to a certain extent of type 1, too:

a) the spread of naturally occuring polioviruses in the years 1957 and 1958.

b) the influence of mass vaccination of the child population with inactivated poliovaccine.

The type distribution of polioviruses (recovered mostly from the poliomyelitis patients) in the years 1956, 1957, 1958 and 1959 in the Czech regions if given in Table 6.

From Table 6 it can be seen that in 1957 type 1 was widely distributed and in 1958 there was a relatively high incidence of type 2 viruses, while no strain of type 3 viruses was recovered in 1958.

We are of the opinion that the spread of naturally occuring polioviruses had a more important influence on the state of seroimmunity (especially to type 1) of the most susceptible groups of children up to 4 years than the mass immunization with Salk vac-

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cine, because, at first, of the fact that no higher incidence of antibodies to type 3 was found in November 1958 when compared to 1957, and, at second, of the results of the analysis of the surveys performed quantitatively (presented in Figures 4-10).

From the lower parts of Figures 4 and 5 it is possible to see a relatively high percentage of children aged 2 to 4 years possessing high titers of type 1 and 2 antibodies, gained in the densely populated region of Usti most probably as a result of a great number of natural infections by type 1 in 1957 and by type 2 of poliovirus in 1958.

Even though there could be established significant differences in the incidence of type 1 and 2 antibodies found in Usti and Jihlava region in 1958, the lower parts of Figures 7 and 8 show that at a lower percentage of children aged 2 to 4 years possessing high levels of type 1 and especially type 2 antibodies was found in Jihlava region than in the region of Usti. Thus, the proportion of children having low levels of antibodies, especially to type 2, was in Jihlava region considerably higher than in Usti region, and on the basis of this finding it is possible to presume that in the more sparsely inhabited rural Jihlava region the child population was not immunized by naturally occuring polioviruses to such an extent as in the region of Usti, and a relatively high percentage of children having low levels of type 2 antibodies could be in the region of Jihlava due to Salk vaccination.

High titers of type 1 antibodies were found in a relatively high percentage of children aged 2 to 4 years in all regions investigated in 1958 (Usti and Jihlava) and in 1959 (Plzen). It is probable that most of the children developed type 1 antibodies as a result of natural infection and not as a response to the Salk

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vaccination.

The influence of the vaccination of a part of the child population with live attenuated polioviruses on the state of seroimmunity to individual types of polioviruses in the regions of Usti and Jihlava can also be seen on Figures 4-9. The lower parts of these figures show the results of the quantitative investigation of pH antibodies in survey made in November 1958, i.e. about 1 month before feeding with type 1 virus was started, and in the upper parts there are shown the results of surveys performed in the same regions in March 1959, i.e. about 1 month after feeding with the last type 2 of the live poliovirus.

When comparing the incidence of poliomyelitis antibodies in 1958 and 1959 in the Jihlava region (Figures 7, 8 and 9) it can be seen that in children up to 2 years,who were not fed with live viruses, a significant increase in type 1 and 3 antibodies, predominantly of high titers, was proved. In type 2 we were not able to demonstrate a significant increase of antibodies in the period from 1958 to 1959, probably because of a high incidence of type 2 antibodies in these age groups already in 1958.

On the other hand, in the region of Usti (Figures 4, 5 and 6) the incidence of antibodies in the youngest children up to 2 years did not change significantly. This finding is probably due to the natural course of immunization of a great part of the population in the densely inhabited industrial region of Usti, in the period of high spread of type 1 and type 2 viruses in 1957 and 1958, respectively.

In the age groups of 2 to 6 years (2 to 8 years,respectively), in which a high percentage of children was fed with three types

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of live polioviruses, a considerably high increase of type 1 and 3 antibodies was observed when comparing the surveys of 1958 and 1959. Only in type 2 this increase is low, which can be explained by the relatively high incidence of type 2 antibody in the population of both Jihlava and Usti regions already in 1958.

It is noteworthy that in spite of feeding only a part of the child population at the age from 6 to 8 years the state of seroimmunity of the whole child population reached during the short winter period a very high level, comparable to the incidence of antibodies in areas or population groups, in which poliomyelitis has had till now endemic character.

On the other hand we were not able to demonstrate a remarcable influence of the vaccination of children with live viruses or the state of seroimmunity of adults.

The comparison of paralytic poliomyelitis morbidity rate in the Czech regions with the susceptibility of the population estimated by serological tests (on the basis of the absence of type 2 neutralizing antibodies), in the corresponding age groups can be seen in Figure 11.

The curves on the left side of Fig. 11 show the paralytic poliomyelitis morbidity rate per 100,000 inhabitants in average values for last 10 years before 1957 and further in 1957 and 1958; the curves on the right side indicate the absence of type 2 antibodies estimated in our 3 consecutive serological surveys (1957, 1958 and 1959).

Up to 1957 the curves indicating the morbidity rate and the absence of type 2 antibodies have a similar course, especially as concerns their drop according to age. Since 1958 there was a great decrease of morbidity and this trend is in a good accordance to

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the drop of the percentage of type 2 antibody absence in the corresponding age groups. These findings bear evidence to the existence of a direct correlation between poliomorbidity and the state of seroimmunity of the population, mainly to the type 2 of poliovirus.

A more detailed elucidation of these correlations would require further more data about distribution of polioviruses in the populations studied at indicated time intervals, similar to those available in our later investigation (as presented for instance in the paper by Burian et all.).

We are of the opinion that one unrepeated serological survey is of a limited value for bringing more light into the still unsolved problems of causes of paralytic poliomyelitis epidemics; for this purpose a long-term recording of poliomorbidity, accompanied by repeated serological surveys and simultaneously performed systematic investigation of the spread of viruses in the population is highly desirable.

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References

1. Skovranek, V., et al.: Journal of Hygiene, Epidemiology, Microbiology and Immunology, 11/4, 415-422, 1958.

2. Skovranek, V., et al.: Ibid, 11/4, 469-477, 1958.

3. Zacek, K., et al.: Ibid, 11/4, 448-456, 1958.

4. Zacek, K., et al.: Ibid, 11/4, 423-437, 1958.

5. Pesek, J., Ibid, 11/4, 443-447, 1958.

6. Vonka, VI, Ibid, 11/4, 457-468, 1958.

7. Skovranek, V., Report Presented at the Fourth International Poliomyelitis Conference, Geneva, 1957.

8. Skovrahek, V. and Zacek, K., Paper Presented at the Sixth Symposium of European Association against Poliomyelitis, Munich, 1959.

9. Skovranek, V., Zacek, K, et al.: Paper presented at the Conference on Live Poliovirus Vaccine, Washington, 1959.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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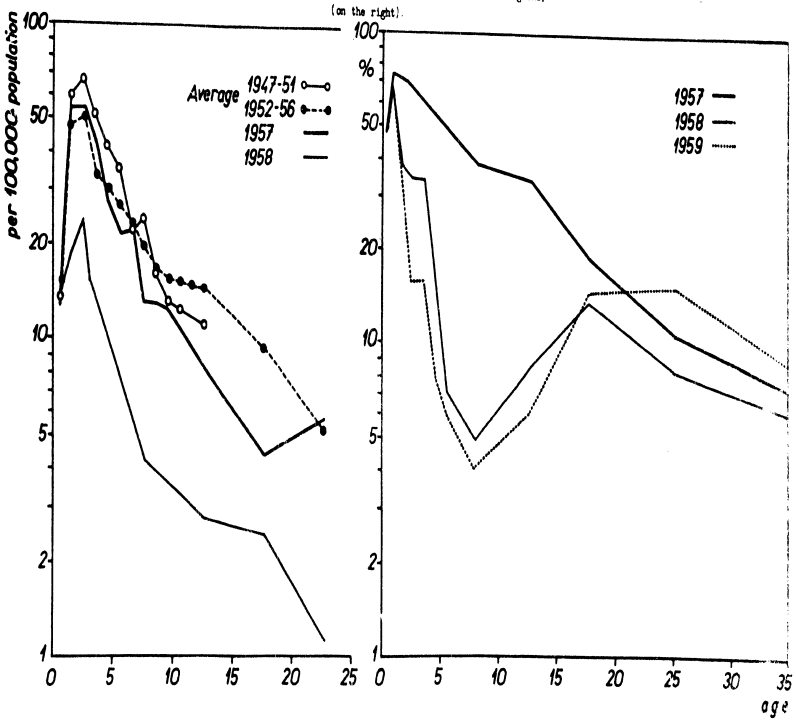
Fig. N 1

MORBIDITY RATE OF PARALYTIC POLIOMYELITIS IN ÚSTÍ AND JIHLAVA REGIONS (on the left) AND ABSENCE OF TYPE 2 ANTIBODIES IN GENERAL POPULATION IN ÚSTÍ AND JIHLAVA REGIONS (average values states for both regions) (on the right).



NOTE: THESE DATA ARE BASED ON THE pH TESTS (1958 and 1959), THE DATA FOR 1957 WERE CALCULATED ON THE BASIS OF THE VALUES FOUND IN CF TEST.

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POLIOMYELITIS ANTIBODIES ESTIMATED IN TWO CONSECUTIVE SEROLOGICAL SURVEYS PERFORMED IN GENERAL POPULATION OF TWO REGIONS.

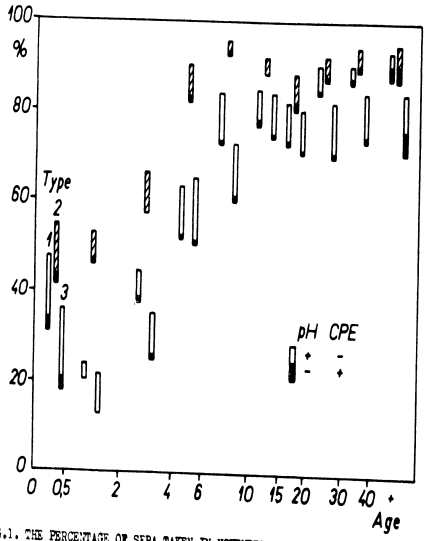

FIG.1. THE PERCENTAGE OF SERA TAKEN IN NOVEMBER 1958, IN WHICH ANTIBODIES WERE DEMONSTRATED IN pH TEST ONLY AND IN CP TEST ONLY.

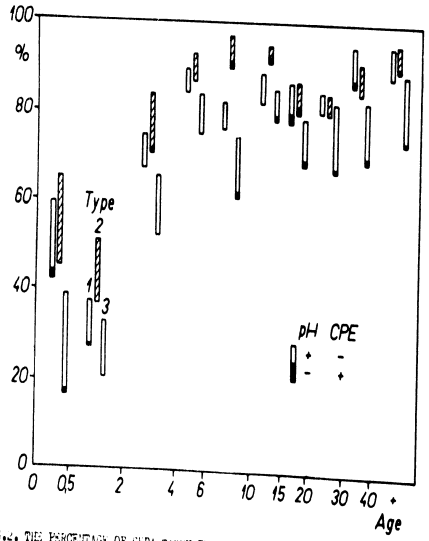

FIG.2. THE PERCENTAGE OF SERA TAKEN IN MARCH 1959, IN WHICH ANTIBODIES WERE DEMONSTRATED IN pH TEST ONLY AND IN CP TEST ONLY.

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Fig. 3

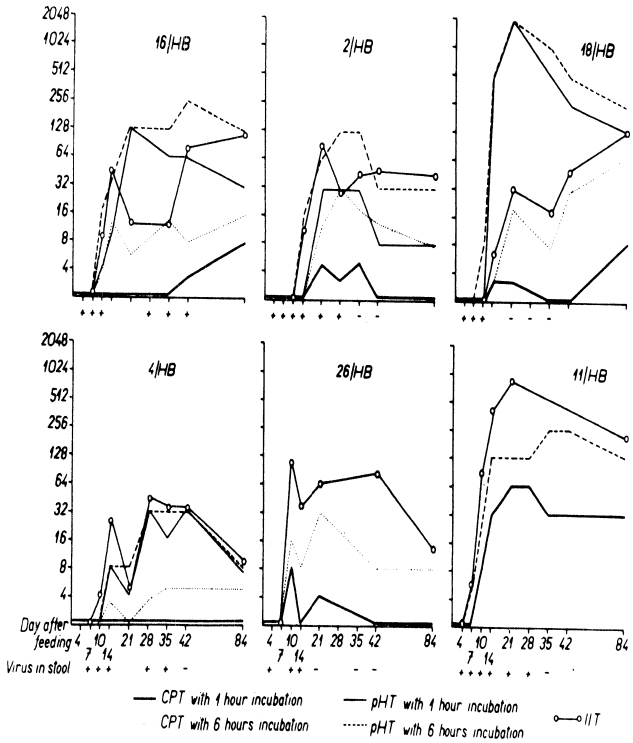

FIG.3. THE DYNAMICS OF TYPE 3 POLIO ANTIBODY DEVELOPMENT ESTIMATED BY DIFFERENT METHODS OF NEUTRALIZATION TEST IN YOUNG ADULTS SIGNOUT PROMULGATING HOMOLOGOUS IMMUNITY FED WITH 100,000 TCD 50 OF TYPE 3 ATTENUATED VIRUS/LEON 1[illegible]

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Fig. 4

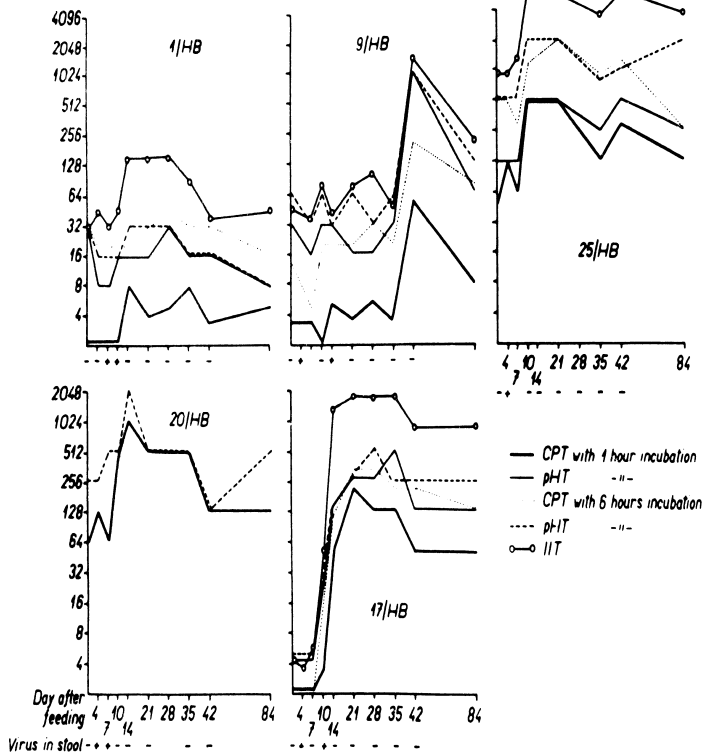

FIG.4. THE DYNAMICS OF TYPE 3 POLIO ANTIBODY DEVELOPMENT ESTIMATED BY DIFFERENT METHODS OF NEUTRALIZATION TEST IN YOUNG ADULTS WITH PREEXISTING HOMOLOGOUS IMMUNITY FED WITH 100,000 TCD 50 OF TYPE 3 ATTENUATED VIRUS /LEON 12 a,b/.

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STATUS OF TYPE 2 POLIOMYELITIS ANTIBODY IN GENERAL POPULATION OF ÚSTÍ REGION.

/ Quantitatively measured by pH test./

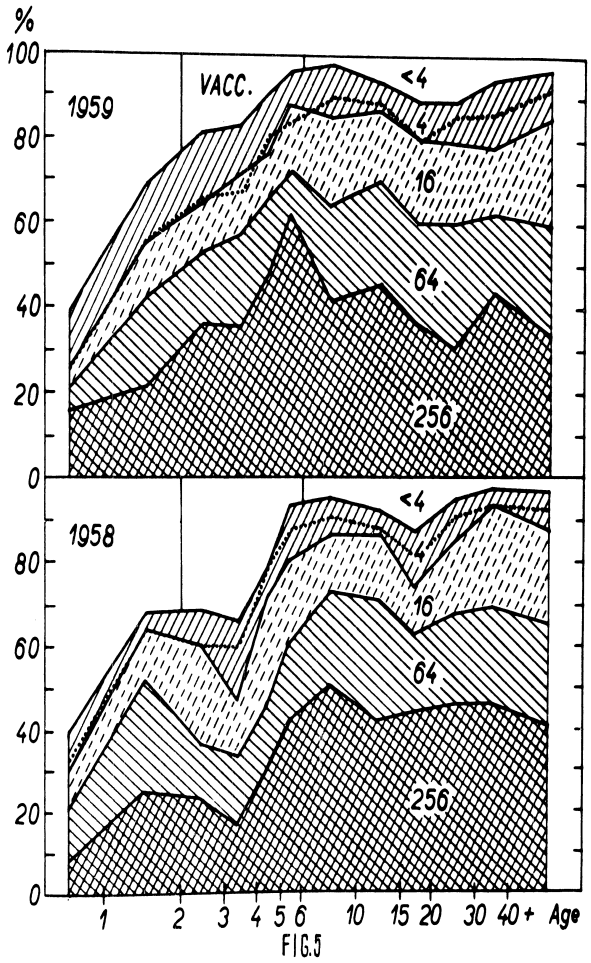

FIG.5

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FIG. 6

[illegible] OF TYPE 3 POLIOMY [illegible] ANTIBODY IN [illegible] POPULATION OF [illegible].

/ Quantitatively measured by [illegible] test./

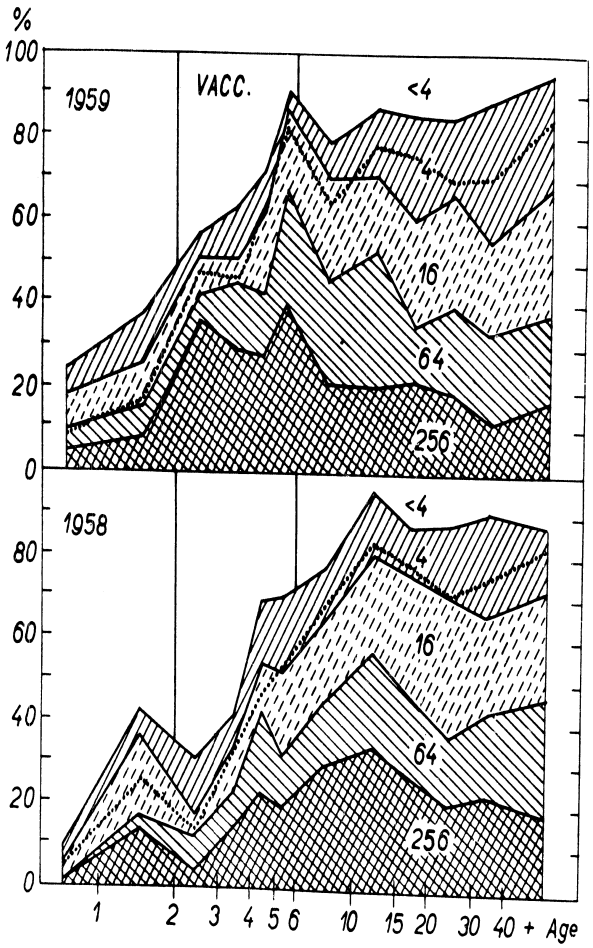

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Fig. 7

STATUS OF TYPE 1 POLIOMYELITIS ANTIBODY IN GENERAL POPULATION OF JIHLAVA REGION.

/ Quantitatively measured by pH test./

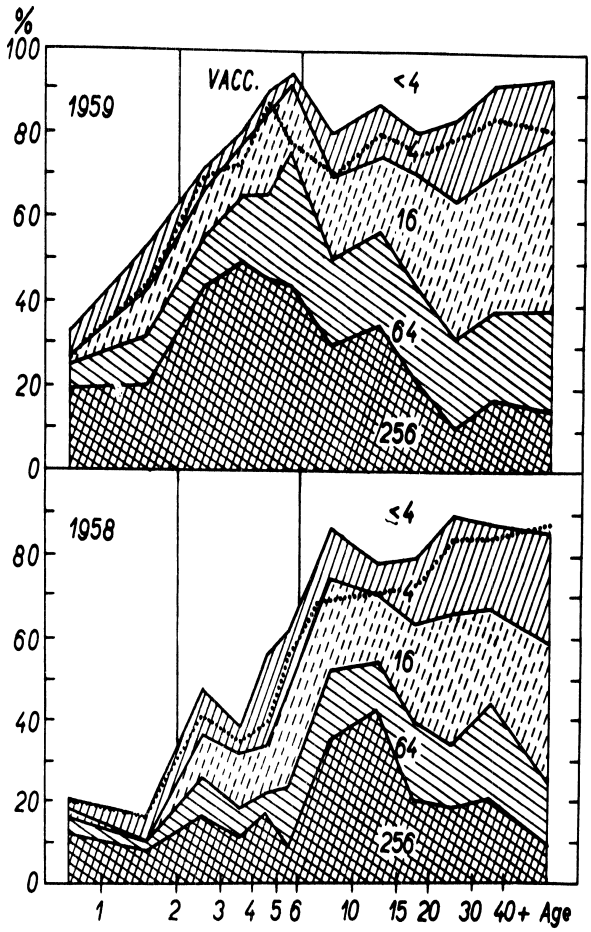

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Fig. 8

[illegible] OF TYPE A NEUTRALIZING ANTIBODY IN GENERAL POPULATION OF JIHLAVA REGION.

/ Quantitatively measured by pH test./

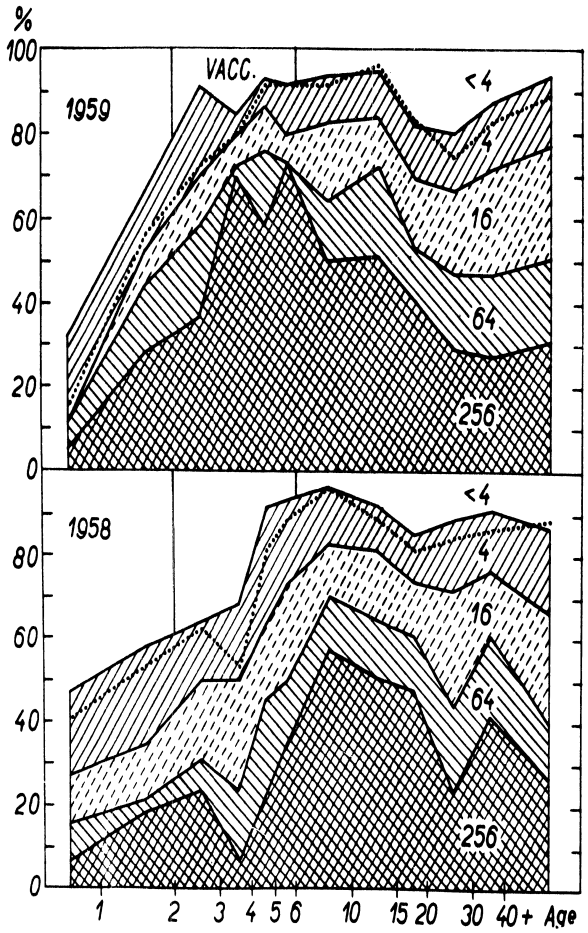

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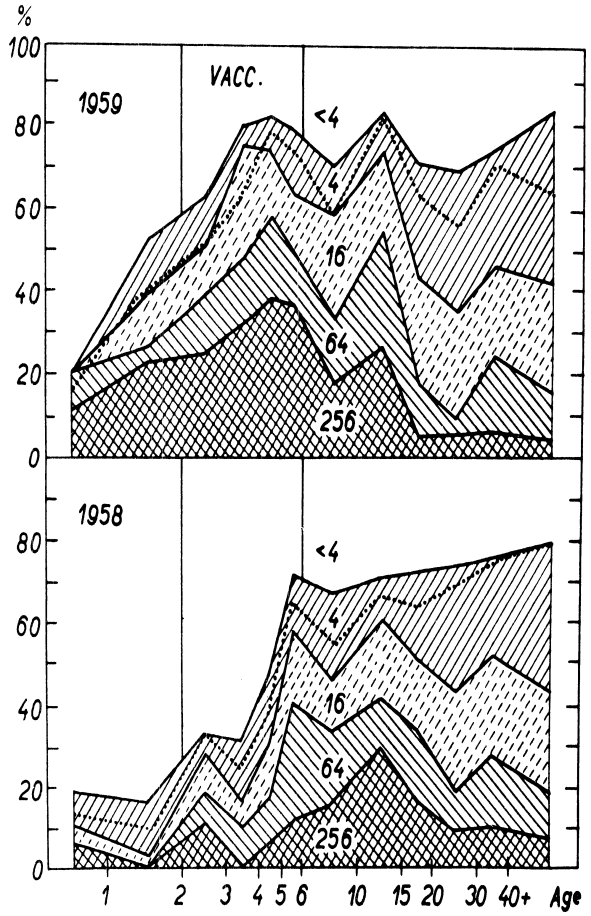
Fig. 9

STATUS OF TYPE 3 POLIOMYELITIS ANTIBODY IN GENERAL POPULATION OF JIHLAVA REGION,

/ Quantitatively measured by pH test./



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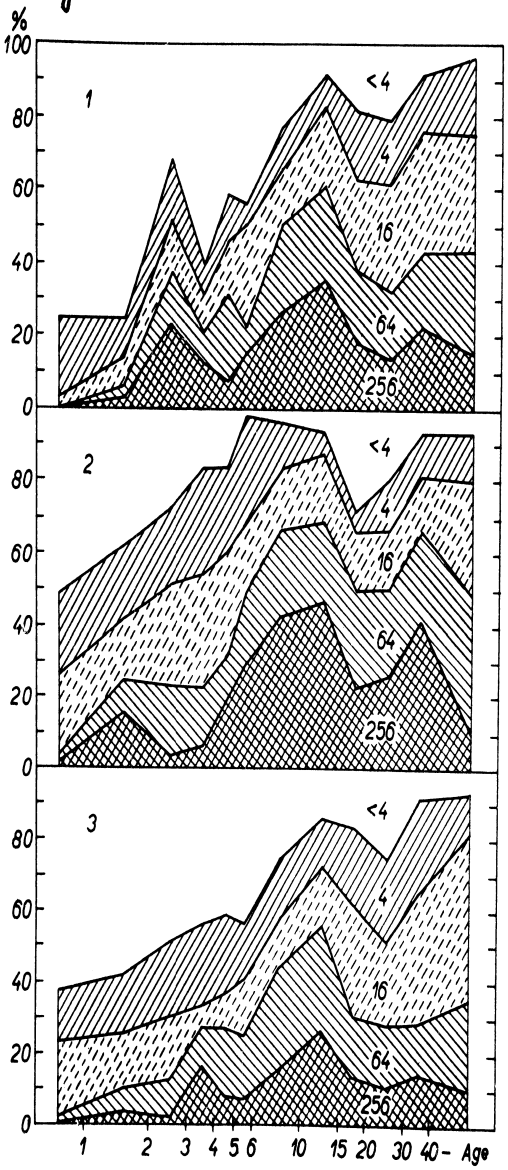
[illegible] ACTIVITY IN ORIGINAL POPULATION [illegible]

Fig. 10 / Quantitatively measured by pH test./



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V.Skovranek et al.,Ministry of Health.

Table 1

Number of Children Vaccinated Against Poliomyelitis with Salk's Vaccine

(Status on July 31,1958)

Age groups:	Injection	Czech regions		Slovakia		Czechoslovakia	
		No.	% population	No.	% population	No.	% population
Preschool age:	1	823,371	93.3	447.485	90.4	1,270,856	92.3
School age: (6-14 ys.)	1	1,069,297	77.6	496,478	78.2	1,525,775	77.8
Preschool age:	2	808,458	91.6	425,203	85.9	1,233,661	89.6
School age:	2	1,052,698	76.4	435,267	74.6	1,487,965	75.9
Preschool age:	3	758,485	86.0	379,386	76.7	1,137,871	82.6
School age:	3	747,785	54.3	295,873	50.7	1,043,658	53.2

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Skovranek, V. et al., Ministry of Health.

Table 2

Basic Data from the Five Investigated Czech Regions

Region	Number of inhabitants on Jyly 1, 1958	Average density of pul. per 1 km^2	Number of patients and polic morbidity (per 100,000 inhab. p.a.)											
			1953		1954		1955		1956		1957		1958	
Usti x)	686,505	166	484	73.1	66	10.0	4	0.6	37	5.5	43	6.3	19	2.8
Liberec	509,944	120	258	51.9	54	10.9	-	-	21	4.2	33	6.5	9	1.8
Jihlava	439,027	66	35	8.1	7	1.6	1	0.2	6	1.4	43	9.8	14	3.2
Ostrava	969,365	214	64	7.0	288	31.6	32	3.4	54	5.7	43	4.4	24	2.5
Total	2,604,841	113	841	33.6	415	16.6	37	1.5	118	4.6	162	6.2	66	2.5
Plzen xx)	580,305	74	64	11.3	20	3.5	12	2.1	25	4.3	27	4.7	12	2.1
All Czech regions incl. investigated regions	9,572,760	122	1895	20.6	794	8.5	133	1.4	388	4.1	639	6.7	231	2.4

Note: x) four regions where Sabin's vaccine was administered.

xx) region where a fourth dose of Salk's vaccine was administered on a mass scale.

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V. Skovranek et al., Ministry of Health.

Table 3

Number of Children in the Four Regions Investigated, by Age Groups, and Number of Children Vaccinated with Three Doses of Salk's Vaccine and Subsequently with Sabin's Vaccine

Age group	No. of children registered x)	Vaccinated 3x with Salk's vaccine		No.of children vaccinated with Sabin's vaccine						Percentage of total no. ++)
				Type 1		Type 3		Type 2		
		No.	%	No	% xx)	No	% xxx)	No.	% +)	
Years										
2-3	44,370	33,179	74.8	24,405	73.6	21,646	88.7	19,192	88.7	45.3
3-4	45,256	40,467	89.5	29,731	73.5	26,409	88.8	23,644	89.5	52.3
4-5	45,734	40,506	83.6	29,967	74.0	26,691	89.1	23,919	89.6	52.3
5-6	46,973	42,104	89.6	29,961	71.2	26,741	89.3	23,631	88.4	50.3
2-6 years total	182,313	156,256	85.7	114,064	73.0	101,487	89.0	90,386	89.1	49.6
6-3 years	100,119	86,310	86.2	29,313	34.0	25,803	88.0	24,124	93.5	24.1
2-3 years total	282,432	242,566	85.9	143,377	59.1	127,290	88.8	114,510	90.0	40.5

Note:

x) children born before Nov. 1, 1956

xx) percentage from no.of children vaccinated 3x with Salk's vaccine

xxx) percentage from number of children which received type 1

+) percentage from no. of children received type 3

++) percentage from total no. of children registered,regardless of vaccination with Salk's vaccine

No. of children vaccinated with type 2 and who were also fed all three types

Numbers and percentages of children vaccinated 3x with Salk's vaccine by July 31, 1958

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Table 4

Status of Poliomyelitis Antibody in General Population of Usti Region
(Qualitatively Measured by CPE and pH tests)

Age group (yrs.)	January-March, 1957							November, 1958							March, 1959						
	No of sera tested	Percentage of triple negatives	Percentage of positive to types					No of sera tested	Percentage of triple negatives	Percentage of positive to types					No of sera tested	Percentage of triple negatives	Percentage of positive to types				
			1	2	3	1,2,3				1	2	3	1,2	1,2,3			1	2	3	1,2	1,2,3
0-0.5								55	29	51	60	38	33	60	20	52	72	42	33		
0.5-1								47	55	17	38	9	4	60	47	22	38	23	10		
1								51	29	41	67	41	29	58	22	41	69	36	16		
2								37	27	46	68	30	22	53	13	66	81	57	47		
3								37	24	46	65	41	27	56	34	75	82	63	46		
4								45	11	65	78	69	45	41	2	83	91	71	64		
5								39	5	69	92	69	56	51	-	92	96	90	81		
6-9		Not done						86	2	79	94	77	66	101	1	86	98	77	67		
10-14								84	-	89	92	95	79	107	0.4	90	93	85	77		
15-19								84	-	80	87	87	63	89	-	88	89	84	86		
20-29								97	-	90	95	88	77	109	0.2	86	89	85	68		
30-39								101	1	93	97	90	84	94	-	96	95	88	80		
40 +								116	-	96	97	88	83	120	-	97	97	95	91		
Total								879						999							
0-0.5	66	33	35	45	27	8		55	42	38	47	16	13	60	45	35	48	22	15		
0.5-1	62	63	11	21	15	2		47	62	11	32	4	-	60	58	20	25	83	3		
1	65	81	22	9	28	-		51	33	33	63	26	16	58	35	21	55	17	5		
2	46	24	35	35	54	9		37	33	35	60	14	5	53	21	59	66	47	36		
3	38	13	42	50	61	16		37	27	43	60	32	19	56	13	68	68	47	32		
4	32	19	59	28	69	16		45	11	58	78	47	25	41	5	71	81	64	44		
5	16	13	25	38	69	6		39	5	64	87	54	44	51	-	86	84	82	61		
6-9	62	16	69	73	71	39		86	4	73	91	69	59	101	2	82	90	64	49		
10-14	90	22	81	80	79	56		84	1	87	92	83	67	107	3	87	89	78	63		
15-19	82	12	73	73	78	38		84	-	75	81	79	50	89	-	88	80	75	50		
20-29	52	-	77	83	79	50		97	-	86	91	71	55	109	2	87	90	73	56		
30-39	227	-	85	89	78	59		101	1	92	93	75	67	94	2	92	86	70	56		
40 +								116	-	95	92	83	72	120	-	96	93	95	76		
Total	638							879						999							

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Table 5

Status of Poliomyelitis Antibody in General Population of Jihlava Region

(Qualitatively Measured by CPE and pH tests)

Age group (yrs.)	No of sera tested	January-March, 1957 — Percentage of triple positive to type					No of sera tested	November, 1958 — Percentage of triple positive to type					No. of sera tested	March, 1959 — Percentage of triple positive to type				
		negatives	1	2	3	1,2,3		negatives	1	2	3	1,2,3		negatives	1	2	3	1,2,3
0-0.5							47	45	38	47	28	17	30	30	54	58	33	30
0.5-1							45	51	20	47	20	11	47	47	32	32	21	11
1							38	40	16	58	16	3	45	22	54	67	54	33
2							42	26	43	64	33	19	43	9	77	86	63	51
3							38	24	37	69	32	18	40	10	80	85	80	70
4							36	3	56	92	47	33	46	2	89	94	83	76
5							34	3	62	94	74	44	50	-	94	92	90	82
6-9		Not done					79	-	87	96	67	60	99	1	79	94	70	56
10-14							85	2	78	92	72	58	76	-	88	95	83	76
15-19							69	1	80	86	72	54	83	1	82	82	71	52
20-29							89	-	90	89	74	56	110	2	84	80	69	54
30-39							89	-	87	91	86	64	76	-	92	88	75	62
40 +							95	1	85	86	80	66	118	-	94	93	83	76
Total							786						893					
0-0.5	79	43	38	32	25	8	47	45	30	43	26	15	54	48	39	41	13	13
0.5-1	72	78	7	10	19	3	45	58	20	40	13	89	53	51	26	15	17	4
1	44	59	14	14	25	2	38	45	16	53	8	3	45	27	45	56	40	20
2	33	42	12	27	49	6	42	29	41	86	33	14	43	14	10	72	51	42
3	25	36	28	36	44	16	38	34	34	53	24	16	40	13	73	80	65	58
4	35	37	23	40	34	9	36	39	89	81	42	18	48	82	87	98	78	72
5	30	24	37	43	47	10	34	12	56	88	65	41	50	-	78	92	74	62
6-9	49	8	53	47	59	10	79	-	75	96	55	41	99	4	71	92	60	46
10-14	69	3	74	49	75	25	85	5	71	88	62	50	76	-	80	96	82	65
15-19	71	-	78	79	76	45	69	1	73	81	65	41	83	1	76	95	63	46
20-29	44	-	82	86	77	57	89	-	84	84	71	48	110	4	78	75	57	39
30-39	32	-	88	88	78	63	89	1	84	86	74	45	76	1	84	83	71	51
40 +							95	1	88	89	79	60	118	2	82	89	65	51
Total	583						786						893					

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Table 6

Distribution of Naturally Occuring Polioviruses in Czech Regions of Czechoslovakia

1956 - 1959

(Viruses Isolated Mostly from the Patients)

Type	1956		1957		1958		1959	
	No	Per cent	No	Per cent	No	Per cent	No	Per cent
1	15	50.0	44	96.3	168	91.8	65	73.7
2	1	3.3	0	0	15	8.2	11	12.5
3	14	46.6	5	3.7	0	0	12	13.8
Total	30		409		183		88	

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Table 7

Status of Poliomyelitis Antibody in General Population in Usti Region

(Quantitatively Measured by pH Test)

Age group	No of sera tested	Poliomyelitis Antibody																	
		Type 1						Type 2						Type 3					
		Negative	Titre pH					Negative	Titre pH					Negative	Titre pH				
		CPE	pH	4	16	64	256	CPE	pH	4	16	64	256	CPE	pH	4	16	64	256
0-0.5	55	62	49	24	16	7	4	53	40	18	13	16	13	83	62	18	11	7	2
0.5-1	47	90	83	9	4	2	2	68	62	11	8	13	6	96	92	4	14	-	-
1	51	67	59	10	10	13	8	37	34	4	12	27	23	75	59	6	19	4	12
2	37	65	54	8	3	11	24	41	33	8	24	14	22	86	70	14	5	8	3
3	37	57	54	3	3	13	27	40	35	19	14	16	16	68	60	8	11	8	13
4	45	42	36	11	11	20	22	22	22	7	27	15	29	53	31	16	11	20	22
5	39	33	31	8	15	31	15	13	15	13	20	18	41	46	31	18	20	13	18
6-9	86	27	21	10	11	19	39	9	6	8	14	22	50	31	23	13	20	15	29
10-14	84	13	11	8	19	31	31	12	8	6	15		41	17	5	15	24	23	33
15-19	84	25	20	8	20	34	18	19	13	13	12	19	43	21	13	12	30	19	26
20-29	97	14	10	8	30	27	25	9	5	10	18	23	44	29	12	17	33	17	21
30-39	101	8	7	8	30	27	28	7	3	4	24	24	45	26	10	24	24	20	22
40 +	116	5	4	13	36	25	22	8	3	10	22	24	41	17	12	16	25	29	18
Total	879																		
0-0.5	60	65	48	37	12	3	-	52	28	38	12	12	10	78	58	25	13	2	2
0.5-1	60	80	78	7	-	2	13	75	62	13	5	5	15	92	77	7	8	5	3
1	58	79	59	22	4	5	10	45	31	14	12	22	21	83	64	12	10	7	7
2	53	42	34	9	6	15	36	34	19	17	11	17	36	53	43	6	9	6	36
3	56	32	25	7	16	13	39	32	18	11	14	21	36	54	38	12	5	16	29
4	41	29	17	7	15	20	41	20	10	15	10	19	46	37	29	10	19	15	27
5	51	14	8	6	18	25	43	16	4	8	16	10	62	18	10	4	20	27	39
6-9	101	18	14	9	21	25	31	10	2	13	21	23	41	36	23	8	25	24	20
10-14	107	13	10	6	17	36	31	11	6	7	16	24	47	22	14	16	18	32	20
15-19	89	16	12	9	24	31	24	20	11	9	19	24	37	25	16	25	26	12	21
20-29	109	17	14	8	26	28	24	15	11	9	19	29	32	30	16	18	27	20	19
30-39	94	8	4	15	35	27	19	14	5	16	16	19	44	30	12	33	21	21	13
40 +	120	4	3	14	35	30	18	7	3	11	26	27	33	15	5	27	30	21	17
Total	999																		

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Table 8

Status of Poliomyelitis Antibody in General Population of Jihlava Region

(Quantitatively Measured by pH Test)

Poliomyelitis Antibody

Age group	No of sera tested	Type 1						Type 2						Type 3					
		Negative	Titre pH 4	16	64	256		Negative	Titre pH 4	16	64	256		Negative	Titre pH 4	16	64	256	
		CPE	pH					CPE	pH					CPE	pH				
0-0.5	47	70	62	13	15	6	4	57	53	21	9	13	4	74	13	19	6	2	-
0.5-1	45	80	80	2	2	5	11	60	53	20	11	9	7	87	80	9	4	-	7
1	38	84	84	5	3	-	8	47	42	24	13	13	18	92	84	13	3	-	-
2	42	60	57	12	5	9	17	38	36	14	19	7	24	67	67	5	9	7	12
3	38	66	63	5	13	8	11	47	31	19	26	16	8	76	68	16	5	11	-
4	36	61	44	22	11	6	17	19	8	28	20	22	22	61	53	16	14	11	6
5	34	44	38	15	23	15	9	12	6	21	23	15	35	35	26	15	18	29	12
6-9	79	25	13	13	23	16	35	4	4	14	13	11	58	45	33	21	13	18	15
10-14	85	29	22	7	15	12	44	12	8	11	16	14	51	33	28	11	19	12	30
15-19	69	28	20	16	25	19	20	19	14	12	13	13	48	35	28	22	17	17	16
20-29	89	16	10	24	32	16	18	16	11	17	28	20	24	29	26	31	25	9	9
30-39	89	16	15	18	24	22	21	13	9	15	16	19	41	26	24	25	23	18	10
40 +	95	13	15	26	34	15	10	12	14	20	26	14	26	21	20	37	25	11	7
Total	786																		
0-0.5	54	61	46	32	9	11	2	59	43	15	24	9	9	87	67	24	5	2	2
0.5-1	53	74	68	6	2	6	18	85	68	20	6	-	6	83	79	-	-	9	12
1	45	56	47	11	11	11	20	44	33	13	9	16	29	60	47	13	13	5	22
2	43	30	23	5	11	12	49	28	14	21	7	21	37	49	37	12	12	14	25
3	40	28	20	3	12	15	50	20	15	5	7	3	70	35	20	5	28	15	32
4	46	13	11	4	20	20	45	9	6	7	11	17	59	22	17	9	15	20	39
5	50	22	6	2	16	32	44	8	8	-	12	6	74	26	10	26	14	12	38
6-9	99	29	21	10	19	20	30	8	6	11	18	14	51	40	31	12	24	15	18
10-14	76	20	12	13	17	22	36	4	5	11	12	21	51	18	17	9	18	28	28
15-19	83	24	18	10	29	22	21	17	18	12	17	12	31	37	29	28	25	13	5
20-29	110	82	16	20	33	21	10	25	20	14	19	18	29	44	31	34	25	5	5
30-39	76	16	18	21	33	21	17	17	12	26	26	20	27	29	26	20	28	18	7
40 +	118	19	6	14	41	25	14	11	7	16	26	20	31	36	17	42	26	11	4
Total	893																		

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Table 9

Status of Poliomyelitis Antibody in General Population in Plzen Region (Quantitatively Measured by pH test)

Age group	No of sera tested	Poliomyelitis Antibody (pH Test) Titre 4	4	16	64	256	Titre 4	4	16	64	256	Titre 4	4	16	64	256
0-0.5	56	57	29	14	-	-	34	35	25	4	2	55	34	7	4	-
0.5-1	62	76	21	3	-	-	52	22	22	2	2	63	14	21	2	-
1	64	75	11	8	3	3	37	20	17	10	16	59	16	16	6	3
2	56	33	16	14	14	23	27	21	28	20	4	48	21	18	11	2
3	48	61	8	10	8	13	17	29	31	17	6	44	23	6	10	17
4	63	41	13	14	24	8	16	24	28	13	19	41	22	10	19	8
5	57	44	5	28	7	16	2	30	19	19	30	41	16	16	17	7
6-9	141	22	11	15	25	17	4	12	18	24	42	26	16	14	28	16
10-14	147	8	8	22	26	36	6	6	18	23	47	14	13	16	30	27
15-19	136	19	18	24	20	19	29	5	16	27	23	17	21	32	17	13
20-29	187	20	18	30	18	14	19	14	17	24	26	25	23	23	18	11
30-39	132	8	15	33	21	23	7	12	15	24	42	8	27	36	15	14
40 +	60	3	22	32	28	15	7	13	32	38	10	6	12	47	25	10
Total:	1209															

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ACADEMY OF MEDICAL SCIENCES OF THE USSR

INSTITUTE FOR POLIOMYELITIS RESEARCH

STAT

Serologic evaluation of various schedules of oral immunization

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During large-scale trials of live poliovirus vaccine in 1959 in our country we obtained numerous serologic and epidemiologic data on practical influence of various schedules of monovaccine administration. The problem of optimal schedule for oral immunization may, no doubt, be solved only after experimental trial of several schedules, various factors being taken into consideration (interference between enteroviruses, season, status of poliomyelitis incidence in a given area and others), which have some effect on the outcome of oral immunization. Therefore the examination of the results obtained, particularly those regarding serologic evaluation of various immunization schedules seems urgent.Up to the present there are differences of opinion as to the schedule of oral immunization. On the one hand, the author of the live vaccine, Dr. Albert B. Sabin, who has established the existence of a certain extent of interference between different types of vaccine viruses when used together, suggested to carry out immunization separately first with type I to be followed by type III and then by type II vaccine with 4 to 6 week intervals.On the other hand, it was found necessary under certain circumstances to shorten the period of immunization and for that reason to give one or two feedings with 4-6 week intervals either of a mixture of all the three types of the vaccine simultaneously or use type I monovaccine to be followed by a combination of type II and III or a mixture of all the three types. Field observations indicated that immunization on shortened schedules gave good results in a number of areas. Their precise evaluation may only be possible by examination of serologic response to vaccination in persons without prevaccination detectable antibody to one, two or three poliovirus types. In 1959 workers of our Institute made observations in different areas of the

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country on the use of the following schedules of feedings with monovaccines in different order or with combinations of live poliovirus vaccine types.

Table 1

Schedules for oral immunization in 1959

Schedules by vaccine types	Number of completely immunized in thousands				
	Estonia	Lithuania	Moscow region	Karaganda	Total
I - III - II	373.8	200.9	-	-	574.7
I - (I+III)- -(I+II+III)	171.1	41.0	-	-	212.1
I - (II+III)	-	10.0	-	-	10.0
II - I - III	19.5	82.4	-	-	101.9
III-I-II	24.9	0.9	-	-	25.8
(I+II+III) one feeding	24.0	84.3	208.0	23.9	340.2
(I+II+III) two feedings	52.1	124.1	850.0	74.2	1100.4
Total	665.4	543.6	1058.6	98.1	2365.1
Incomplete schedules	30.2	18.8	-	-	49.0
Total	695.6	562.4	1058.0	98.1	2414.1

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Serum specimens of more than 1500 persons from republics and regions indicated in Table I were tested in three laboratories of the Institute for Poliomyelitis Research.

This communication presents still incomplete materials of serologic investigations in neutralization tests of blood specimens before and after vaccination. Our method of antibody titration by pH test was in its main features that of Melnick and Opton, but the pH test was more frequently done in tubes under vaseline oil. Smaller number of the tests was done in plastic panels with cups.

The Tables present results of serologic survey of only those persons who had no detectable antibody (in serum dilution 1:2) before vaccination. Blood specimens were collected, as a rule, one month after first feeding and one to two months after two or three feedings.

As may be seen from the Tables, with all schedules of monovaccine alteration or combination antibody development de novo to the homologous type was observed in 55 to 90 per cent one month after the first feeding.

These results, as a rule, considerably improved by the time the third blood specimen was collected (that is, one month after two or three feedings). For example, one month after feeding with type I vaccine homologous antibodies were found in 60.7 per cent vaccinated, and three months later in the same persons without additional administration of type I vaccine the percentage of positive responses rose to 89.9 with considerable rise in antibody titers. Consequently, for type I antibody it is advisable to evaluate the results with a third blood specimen.

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Table 2

Dynamics of poliomyelitis antibody response in children under 3 years one to three months after the beginning of live poliovirus vaccination (schedule: types I - III - II) in Estonian SSR (pH color test. Dobrova, I.N., 1959)

Groups before vaccination (without antibody)	Total number of children	no antibody response	Acquired antibody	including children with antibody in titers		
				4-32	64-128	256+
One month after the first feeding						
I°	79	31	48	23	15	10
		39.3	60.7	29.1	19.0	12.6
Three months after the beginning of vaccination						
I°	79	8	71	31	18	22
		10.1	89.9	39.2	22.8	27.8
II°	54	1	53	10	8	35
		1.9	98.1	18.5	14.8	64.8
III°	97	12	85	18	20	47
		12.4	87.6	18.5	20.6	48.45

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Table 3 presents comparison of the results of immunization with separate monovaccines

Table 3

1. One month after the first feeding (Estonian SSR)

	I-III-II			I-(I+III)-(I+II+III)			II-I-III			III-I-II		
	Without prevaccination antibody	Antibody response No.	%	Without prevaccination antibody	Antibody response No.	%	Without prevaccination antibody	Antibody response No.	%	Without prevaccination antibody	Antibody response No.	%
I	215	152	70.7	25	16	64.0				7	2	28.6
II	138	76	55.1	17	6	35.3				8	4	56.0
III	215	46	21.4	30	6	20.0				13	12	92.3

2. One month after three feedings (Estonian SSR)

	I-III-II			I-(I+III)-(I+II+III)			II-I-III			III-I-II		
I	142	124	87.3				17	15	88.2	28	16	72.7
II	115	109	94.8				5	4	80.0	20	18	90.0
III	157	148	94.3				15	12	80.0	27	23	85.2

3. One month after three feedings (Lithuanian SSR

	I-III-II			I-(I+III)-(I+II+III)			III-I-II		
I	20	14	70.7	25	23	92.0	28	25	89.3
II	13	10	76.9	21	19	90.5	17	16	94.1
III	12	10	83.3	27	17	100.0	25	13	92.0

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It should be mentioned that perhaps because of latent type II virus carriage we found in the second blood specimen type II antibody in a considerable proportion of cases despite the fact that we fed with type I vaccine (see Table 3, upper left side).

Table 4

(Trivalent vaccine, one feeding)

Antibody response one month after one feeding of trivalent live poliovirus vaccine in children without prevaccination antibody

	Estonian SSR			Lithuanian SSR			Moscow region		
I	57	38	66.7	28	25	89.3	100	59	59.0
II	35	31	88.6	17	16	94.1	79	66	83.5
III	48	36	75.0	25	23	92.0	112	66	58.9
	Including groups of "triple-negative" children								
I	24	13	54.2	3	2	66.7	46	22	47.8
II	24	21	87.5	3	3	100.0	46	36	78.3
III	24	17	70.8	3	3	100.0	46	19	41.3

(Trivalent vaccine, two feedings)

Antibody response I month after two feedings (with monthly interval) of trivalent live poliovirus vaccine in children without prevaccination antibody

	Estonian SSR			Lithuanian SSR		Moscow region
I	51	39	76.5	16	9	56.2
II	35	30	85.7	9	9	100.0
III	73	65	89.0	8	6	75.0
	Including groups of "triple-negative" children					
I	25	19	76.0	2	2	
II	25	22	88.0	2	2	
III	25	20	80.0	2	1	

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Note: 1) Tests were done: with Estonian sera by Dobrova, I.N.; with Lithuanian sera by Yankevitch, O.D.; with sera from Moscow region by Voroshilova, M.K., Taranova, G.P.

2) In each section:

first column - number of children without homologous antibody before vaccination

second column - number of children developing antibody as a result of vaccination

third column - per cent of positive responses.

In Table 4 results of survey of children immunized orally with trivalent live vaccine are compared. It is noteworthy that in Moscow region results for type I and type III antibody were much lower than those in Estonia and Lithuania. We explain it by the fact that in Moscow region vaccinations were carried out in summer when large number of enterovirus carriers was reported. Interference with enteroviruses prevented antibody response to type I and III, and to a lesser extent to type II.

Comparison of Tables 3 and 4 reveals a definite, though not very significant (in terms of antibody response rate) superiority of the first and the second immunization schedules over other schedules. But considering the gain in time of vaccination with trivalent vaccine we believe that this schedule must also be used both in pre-epidemic season and for rapid revaccination on epidemiological indications.

Different schedules should be varied depending on current epidemiological circumstances, with their advantages being flexibly used.

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In accord with the approved instructions the main schedule Is schedule I (types I-III-II) to be followed by revaccination with trivalent mixture 2-3 months to 1.5 years after the first course.

This recommendation is correct. In a number of republics revaccination is given two times, at first with type I vaccine and in six weeks with trivalent mixture.

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INSTITUTE FOR THE STUDY OF POLIOMYELITIS

STAT

THE INTENSITY OF IMMUNOLOGICAL CHANGES IN CHILDREN INOCULATED WITH LIVE VACCINE AGAINST POLIOMYELITIS WITH DIVERSE SCHEMES OF IMMUNIZATION

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1. Consecutive three=fold immunisation of receptive children with monovalent preparations of live vaccine against poliomyelitis of the I,II and III types secures comparable indices for qualitative rise in the number of antibodies,, regardless of the successive order in which individual vaccine serotypes are employed. Notice is taken of regular lagging behind of the indices showing the number of antibodies against the virus of the III type, as contrasted to those indicative of humoral immunity against the types I and II.

2. Groups of children who failed to respond by the devel ment of humoral immunity to a single administration of monovalent vaccines constitute about 10% for the vaccines of the I and II types and around 20% for that of the III type. Therefore, children subject to three=fold inoculation with polyvalent vaccine of the I,II and III types should be revaccinated, since this eliminates the defects of the first immunization round and helps to produce in most of the refractory children the state of complete immunity with respect to all of the three types.

3. Prepared polyvalent vaccine, containing 400 000 TCD_{50} of the each vaccine type, represents most practicable kind of a single preparation, which with three=fold immunisation increases the cost of inoculation by 1/3 as compared with four= fold vaccination with monovaccines and trivaccine.

Single introduction of trivaccine stimulates a somewhat lower antibody level to all the three types, when compared with three=fold introduction of monovalent vaccines. But repeated and, especially, three=fold administration of trivaccine ensures well= pronounced immunological changes nearly in 100% of the children.

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5. Of an exceptional value with regard to its speed and efficacy is the three=fold immunization carried out according to the following scheme: monovaccine of the I type, divaccine of the II and III types, trivaccine of the I,II and III.types,- all of these inoculated with an interval of I month. This scheme secures maximal immunological effectivness, with the same amount of preparation as required in the instance of three= fold introduction of the monovaccine with revaccination with trivaccine after lapse of 1-3 months. Its great merit lies in the acceleration of the entire vaccination cycle and in that it precludes engaging of the medical staff in the fourth revaccination.

6. Within the periods embracing 24 months of observations the postvaccinal immunity was seen to remain on a high level.

7. A large=scale serological examination of susceptible children of all ages in the Bialorussian Moldava,Latvian republics, and also in the Novgorod and Pskov regions, effected before and after immunization with live vaccine, has established radical changes in the immunological age structure, consequent upon immunization. If prior to vaccination over 25% of pre= school children were susceptible to one of the three types of poliomyelitis virus - in 6-12 months after two=fold immunization with the vaccine of the I type and divaccine of the II and III types the number of susceptible children decreased down to 5-10%, while upon termination of the third immunization with trivaccine the figure representing insusceptible children was near 100%.

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9. The success of vaccination is, in the main, dependent upon the dose of the preparation actually introduced and on the state of specific and non-specific immunity of children undergoing inoculation.

9. The introduction into the intestinal canal of attenuated strains of the poliomyelitis virus belonging to the I, II and III types has as its result the development of a lasting resistance to repeated infection with homologous viruses.

No difference could be noted between the intensity and duration of local resistance of the intestinal tract in children subject to inoculation with live vaccine of various serotypes. In this respect the III virus type which is prone to less regularly stimulate accumulation of specific antibodies proved fairly active in producing local resistance of the intestinal tract.

10. The resistance of the intestinal canal to repeated infection sets in already in 1 month following vaccination and is retained without substantial changes for a space of 6 months-2 years, with the initial dose comprising 100 000 - 1 million TCD_{50}.

11. The resistance of the intestinal tract in children to the primary introduction of vaccinal strains is distinctly related to the state of their humoral immunity to the homologous virus. It has been noted that the intestinal tract is poorly protected against its invasion by vaccinal strains with low initial titers of virus-neutralizing antibodies /1:4-1:16/, while elevated titers of antibodies either totally precludes reproduction of vaccinal strains or make their development weak and short-lived.

12. To produce lasting and intensive resistance /local/ of the intestinal tract it is important to secure garanteed vac-

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cination with an adequate vaccine, taking account of the unreliable nature of immunization developing as the results of contacts with vaccinated children.

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Serologic investigations in connection with mass oral immunization with live poliovirus vaccine carried out during a period of increased poliomyelitis incidence in Tashkent

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In the summer of 1959 increased poliomyelitis incidence in Tashkent was recorded which turned into an outbreak. Children of younger age-groups were predominantly affected.

At the time when the increase in the number of cases became menacing, mass poliomyelitis immunization of children

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was carried out. On the suggestion by Prof. M.P. Chumakov the immunization was done orally with liquid trivalent live vaccine from Sabin attenuated strains prepared in Moscow at the Institute for Poliomyelitis Research, Academy of Medical Sciences of the USSR.

The vaccine was given to children up to 15 years of age inclusive.

40-45 days after the first feeding a second one was given also with trivalent vaccine.

It is not our task to analyse the epidemiologic effectiveness of the vaccine, because it is the subject of a separate paper. We shall stick to analysis of immunologic reaction in the vaccinated by means of serologic methods.

Before the first feeding we collected sera from 325 children who had never had any poliomyelitis vaccination. These children were from 8 children's institutions in Tashkent. The ages are given in Table I.

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Table I

Age of the children surveyed

Age	Number of children	Age	Number of children
Under 6 mo.	17	10-11 yr.	20
6 mo.- 1 yr.	15	11-12 "	16
1 - 2 yr.	27	12-13 "	18
2 - 3 "	17	13-14 "	21
3 - 4 "	27	14-15 "	24
4 - 5 "	17		
5 - 6 "	27		
6 - 7 "	27		
7 - 8 "	16		
8 - 9 "	16		
9 -10 "	20		

Second blood specimens were collected from the same children 30-35 days after the first feeding. 30 days after the second feeding third blood specimens were collected.

Serum specimens were also collected from children immunized with trivalent live vaccine during the incubation period or from those who had not responded to vaccination and developed poliomyelitis.

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Paired and tripled sera were heated at 56°C for 30 minutes and stored at -20°C until simultaneous use in cytopathogenic neutralization test.

It should be noted here that for some technical reasons or others not all the sera collected could be used in tests.

The tests were carried out in monolayer trypsinized kidney monkey cell cultures and in fibroblast cultures of tripsimized skin-muscle human embryonic tissue. For monkey kidney cells a medium was used containing lactalbumin hydrolyzate in Hanks' solution and bovine serum. Before inoculation this was changed for medium 199. The fibroblasts were grown before and after inoculation with the virus in medium 41.

Sabin attenuated strains of the 3 types of poliovirus were used in the test. The titers of the virus were checked in tissues taken for the given test. Sera in dilutions of 1:4, 1:8, 1:16, 1:32, 1:64, 1:256 and 1:1024 were tested against 100 TCD_{50} of the virus.

The neutralization test was done according to the generally accepted method. The results were read at 6 days.

For obtaining data on prevaccination immunologic status of the population surveyed sera collected before vaccina-

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tion were tested in 1:4 dilution in preliminary neutralization test (later the same sera were tested in extensive neutralization tests simultaneously with paired samples).

The results of this experiment are presented in Table 2

Table 2

Lack of poliovirus neutralizing antibodies in children of Tashkent before mass oral immunization with trivalent live poliovirus vaccine

Age-groups (years)	Number of sera	Number of sera without antibody types						Including triple-negative		Intensive incidence rate per 100,000
		I		II		III				
		No.	%	No.	%	No.	%	No.	%	
0-2	45	34	75.5	33	73.3	34	75.5	27	60.0	484
2-5	50	15	30.0	13	26.0	12	24.0	5	10.0	210
5-10	97	8	8.2	6	6.2	16	16.5	0	0.0	35
10-15	97	15	15.4	1	1.0	6	6.2	0	0.0	9
Total	289	72	24.9	53	18.3	68	23.5	32	11.0	139

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The age-groups shown in the Table were composed on the basis of age-specific incidence rates observed during the epidemic outbreak in Tashkent. A total of 289 first serum specimens were tested. Of children under two years 75.5 per cent had no type I poliovirus antibody, 73.3 per cent had no type II antibody and 75.5 per cent no type III antibody; of children of 2 to 5 years 30.0 per cent had no type 1 antibody, 28.0 per cent had no type II antibody and 24.0 per cent no type III antibody. The corresponding figures for children of 5 to 10 years old were 8.2, 6.2 and 16.2 per cent; for children of 10 to 15 years old 15.4, 1.0 and 6.2 per cent. In the age-group under 2 there were 60.0 per cent triple-negatives and in the age-group of 2 to 5 10.0 per cent triple-negatives.

It is noteworthy that the least protected (by serologic evidence of immunity) age-group of children under 2 had the heaviest incidence (intensive incidence rate per 100,000 for this group was 484).

For the definition of immunologic effectiveness of one feeding of the vaccine 239 paired serum specimens were tested. Development and rise of neutralizing antibodies to all three types of the virus was observed. For example, of the formerly negative children 91.8 per cent developed antibody

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to type I, 83.7 per cent to type II and 69.5 per cent to type III (Table 3).

Table 3

Antibody response to types I, II and III poliovirus after one feeding with trivalent live poliovirus vaccine

Prevaccination titer	Number of persons tested	Number of persons with type I antibody response and rise of titer		Number of persons tested	Number of persons with type II antibody response and rise of titer		Number of persons tested	Number of persons with type III antibody response and rise of titer	
		No.	%		No.	%		No.	%
negative									
<4	61	56	91.8	43	36	83.7	59	41	69.5
4-32	124	90	72.5	136	93	68.3	137	74	54.0
64-256	38	17	44.7	44	25	56.8	37	22	59.4
1024	16	-x)	-	16	-x)	-	6	-x)	-
Total	239	163	73.0xx)	239	154	69.0xx)	239	137	58.8xxx)

x) Antibody rise in serum dilutions higher than 1:1024 was not tested.

xx) Calculated for 223 sera (163/223 and 154/223)

xxx) Calculated for 233 sera (137/233).

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Thus the proportion of children responding with development or rise of antibody titer to type I was 73.0 per cent, to type II - 69.0 per cent and to type III - 58.8 per cent.

Table 4 presents data on the dinamics of antibody rise in children previously negative to any one type.

Table 4

Dynamics of antibody response after one feeding with live poliovirus vaccine in children without antibodies to homologous type of virus before vaccination

Antibody titer (serum dilutions)	Number of sera with indicated titer after vaccination		
	type I	type II	type III
<4	5	7	18
4	4	0	8
8	5	1	13
16	8	6	4
32	12	4	4
64	14	9	2
256	6	9	5
1024	7	7	5
Total	61	43	59
Geometric mean titer	37	49	10

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Similar data for triple-negative children are given in Table 5.

Table 5

Dynamics of antibody response in triple-negative children after one feeding with live poliovirus vaccine

Antibody titer (serum dilutions)	Number of sera with indicated titer after vaccination		
	type I	type II	type III
<4	2	6	9
4	2	0	2
8	2	0	5
16	3	2	1
32	7	3	2
64	6	5	2
256	3	7	2
1024	1	3	3
Total	26	26	26
Geometric mean titer	34	39	8

Of the 26 children examined who had been triple-negative before vaccination, 24 developed type I antibody, 20 type II antibody and 17 type III antibody after one feeding of the vaccine.

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Of the total number of 239 children tested after one feeding one remained triple-negative (child Z-v, 2 years old, with abnormal nervous system development), 6 acquired antibodies to one type of the virus, 23 to two types and 209 to all three types (Table 6).

Table 6

Antibody response to the three types of the virus after one feeding with trivalent live poliovirus vaccine

	Number	Number triple negative	Number with antibodies to one	to two	to three
Before vaccination	239	26	18	49	146
After vaccination	239	1	6	23	209

Furthermore 112 triple sera collected before vaccination and after the first and the second feedings, were examined in the neutralization test. After the second feeding 109 of 112 children had antibodies to the three types and 3 children had antibodies to two virus types (Table 7).

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Table 7

Antibody response after two feedings with trivalent live poliovirus vaccine

	Number tested	Number triple-negative	Number with antibodies to one type	to two types	to three types
Before vaccination	112	6	9	19	78
After one feeding	112	-	1	7	104
After two feedings	112	-	-	3	109

The second feeding produced antibodies in a number of children who had not responded to the first one and led to their exclusion from the group of triple-negatives. At the same time the second feeding didn't entail further rise in antibody titers in children responding to the first feeding (Table 8).

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Table 8

Neutralizing antibody titer in children examined before vaccination and after the first and the second feeding with trivalent live poliovirus vaccine

	Number tested	Type I antibodies				Type II antibodies				Type III antibodies			
		<4	4-32	64-256	1024 a.>	<4	4-32	64-256	1024 a.>	<4	4-32	64-256	1024 a.>
Before vaccination	112	24	61	19	8	14	70	19	9	17	67	24	4
After one feeding	112	-	50	42	20	2	52	40	18	7	63	30	12
After two feedings	112	-	53	41	18	-	58	42	12	3	79	22	8

Discussion

Immunologic status before vaccination was studied in children from boarding children's institutions. There may arise some doubts whether the findings obtained would be shared by other groups of children. The conformity between the data on the lack of antibody by age-groups and on incidence rates for all contingents of children, however, allows to extend the significance of these findings though not without some reservations.

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Our data prove the immunologic effectiveness of the live vaccine used under conditions of an epidemic in progress. Feedings of the trivalent live vaccine produced development and rise of antibody to all the three types of poliovirus in the majority of cases. This points to the absence of competition between the vaccine viruses and, on the other hand, a possible interference of the attenuated viruses with "wild" viruses circulating in the surveyed communities.

This assumption may be confirmed by reference to the findings in children vaccinated in the incubation period and then developing poliomyelitis. By the time of convalescence most of these children had type I antibody in high titers. Titers of type II and, especially, type III antibody were much lower. Over 30 per cent of children had no type II antibody and about 50 per cent had no type III antibody (according to preliminary data of M.K. Voroshilova and ours). Inhibition of types II and III antibody development may, perhaps, be explained by interference with "wild" type I virus which was the main responsible agent of the outbreak in Tashkent (according to S.S. Maxumov's data). In these cases the attenuated viruses were overcome by the "wild" virus, the phenomenon not observed in normal children examined.

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We have no materials directly indicating the extent of the influence of "wild" viruses disseminated by carriers on post vaccination rise of antibody titers. Simultaneous development of antibodies to the three types of poliovirus may be considered as an argument against any significant part of the "wild" virus in response of children to vaccination. At the same time a comparatively active response to type I may be explained not only by certain activity of the attenuated virus of this type but also by additional effect of the "wild" virus.

Under our circumstances a second feeding has not produced any rise in antibody titers obtained as a result of the first feeding. There are indications in literature of the inhibition of vaccine infection and of poor and short-time multiplication of the vaccine virus on repeated administration of the live vaccine. It is possible that stable antibody titers which we observed may be explained by the immunity of susceptible cells of the intestinal tract preventing accumulation and assimilation of the vaccine antigen. If this is the case, stability of antibody titers on repeated oral immunization may be considered as a measure of intensity of the immunity obtained. At the same time our observations showed that there were refractory children

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responding not at all or poorly to one feeding. Taking this into account it should be considered advisable to carry out repeated immunizations with the live vaccine.

Conclusions

1. Comparison of data on the lack of antibody in children of different age-groups and incidence-rates reveals correlation between them.

2. Oral immunization with trivalent live poliovirus vaccine carried out during an epidemic outbreak of poliomyelitis produced development and rise of neutralizing antibody titers to all the three types of poliovirus in the great majority of the children examined.

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IMMUNOLOGIC SHIFTS IN CHILDREN IMMUNIZED WITH LIVE POLIOVIRUS VACCINE

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This communication presents the results of serological investigations on live poliovirus vaccine carried out at the Institute of Microbilogy, Academy of Sciences of Latvian S.S.R.

The objectives were to study immunological shifts in blood of children vaccinated with live poliovirus vaccine.

Serological investigations involved children of 0 to 8 years of age vaccinated orally with monovaccines containing 100,000 TCD_{50} of attenuated poliovirus strains. Blood specimens were collected from cubital vein or, in infants, from temporal vein in amounts of 3-4 ml. Blood collections were made before and 4 weeks after each feeding with monovaccines and 4 weeks after last feeding. In some children blood specimens were taken 7 months after last feeding to study remote results of immunization.

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Methods

Virusneutralizing poliomyelitis antibody were determined by pH color test in human amniotic cell cultures. Titrations were done in serum dilutions I:4, I:16, I:64, I:1024, I:4096.

100 TCD_{50} of poliovirus of all the three types were taken (strains Brunhilda, MEF-I and Saukett of types I,II and III, respectively).

Results

Of 166 children of 0 to 8 years examined there were 25 children without antibody to any one of poliovirus types before immunization. Nineteen of these triple-negative children were immunized with monovaccines on the schedule type I followed by type III and then by type II and 6 children on the schedule type III - type I - type II.

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As is seen in Tables I and 2 all 25 triple-negative children after immunization with monovaccines of the three types developed virusneutralizing poliomyelitis antibody to all the three poliovirus types. Four weeks after feeding with monovaccine most of the children responded with development of homologous antibody and in a number of cases heterologous antibody as well. Only six children four weeks after feeding with type I monovaccine had no detectable serum antibody to any one type of poliovirus including type I. Four weeks after feeding with type III monovaccine only one of these 6 children had detectable antibody to types I and II polioviruses. And only after feeding with last, type II monovaccine, did antibody begin to develop in these children. Sixty days after the end of the vaccination cycle all these six formerly triple-negative children had detectable antibody to all three poliovirus types.

After ingestion of monovaccine of the appropriate type most rapid and extensive antibody response to type II is observed. After ingestion of type I monovaccine most of the children develop heterologous type II antibody. Antibody to types I and III poliovirus develop much slower and in lower titers.

Table 3 presents data on rate of antibody titer increase to individual poliovirus types in triple-negative children vaccinated on the schedule type I - type III - type II. In most of the triple-negative children examined (I5 of I9) type I antibody titer increased 4-fold and I6-fold.

More extensive antibody response was observed to type II.

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In I3 of I9 children antibody titer increased 64-fold and greater after vaccination. In I5 of I9 children type III antibody titer increased 4-fold and I6-fold. Rate of antibody increase in children possessing antibody as a result of natural or artificial immunization is shown in Table 4.

As may be seen in Table 4, the majority of I45 children examined responded to vaccination with marked increase in poliomyelitis antibody titers. Of 37 children under three years only one had no rise in type I antibody titer, three had no rise to type II and three to type III antibody.

Among pre-school children the number without antibody rise was somewhat greater. Thus, of 35 children of 4 to 5 years of age examined, nine had no rise of type I antibody, 6 to type II antibody and I3 to type III antibody. In nursery children more extensive antibody development after immunization is observed, especially to type II virus. Thus, of 37 children under 3 years examined, 64-fold rise of type II antibody was observed in 25 children, to type I antibody in 20 children and to type III in 20 children. Of 35 children in the age-group 4 to 5 years 64-fold or greater rise in titer to type I antibody was observed in 8 children, to type II in I3 children and to type III only in two children. A similar picture was observed in children of 6 to 7 years of age.

Irrespective of the schedule of immunization with mono-vaccines and the age of vaccinees in all cases we observed more extensive antibody response to type II.

Examination of our data did not reveal any superiority in the effectiveness of any of the immunization schedules tested.

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Eleven children vaccinated with type I followed by type II and then by type III were bled 6 months after the last feeding. The results of examination of their serum specimens indicate that levels of antibody to all three types have not changed and in some of the children there was even rise in type III antibody titers which may, perhaps, be explained by the fact that type III monovaccine was fed last.

Conclusions

I. Examination of the children immunized with monovaccines containing attenuated poliovirus strains of each of the three types demonstrated regular increase of antibody titers to all three poliovirus types.

2. Use of different schedules of monovaccine feedings at 4 week intervals (I-III-II, III-I-II; I-II-III) did not show any superiority in the effectiveness of any of these immunization schedules.

3. More extensive antibody response in the process of immunization is observed in children of younger ages (0 to 3 yeus) compared to preschool children. Among children of 4 to 8 years of age reduction in number of seronegative is much slower in the process of immunization than among children of 0 to 3 years.

4. Irrespective of immunization schedule and age of vaccinees, most extensive antibody response to type II poliovirus is observed.

5. Immunologic shifts in children vaccinated with live poliovirus vaccine are persistent. Six months after immunization antibody levels did not decline.

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Table I - Antibody response in triple-negative children immunized with live vaccine

Initials and age of children	Before vaccination			4 weeks after feeding with monovaccines									60 days after vaccination			
				Type I			Type III			Type II						
B.V. 6 yr.	0	0	0	I6	I6	0	I6	256	0	I6	256	I6	I6	256	64
B.L. 5 "	0	0	0	I6	0	0	I6	256	0	I6	256	I6	I6	256	64
Z.V. 7 "	0	0	0	I6	I6	0	I6	256	0	I6	256	64	I6	I000	256
K.T. 7 "	0	0	0	I6	I6	4	I6	I6	64	I6	64	64	I6	64	64
K.V. 6 "	0	0	0	0	0	0	0	0	0	4	4	4	4	I6	I6
N.A. 5 "	0	0	0	0	0	0	0	0	0	0	0	0	4	64	4
P.I. 7 "	0	0	0	0	0	0	0	0	0	4	64	0	4	64	I6
Ch.T. 5 "	0	0	0	I6	256	64	64	256	64	64	I000	64	64	I000	256
Ya.E. 5 "	0	0	0	256	256	0	256	4000	64	256	4000	4000	4000	4000	4000
G.Z. 7 "	0	0	0	0	0	0	4	I6	0	64	64	I6	64	I6	I6
S.V. 7 "	0	0	0	I6	4	4	-	-	-	256	256	64	256	256	74
K.V. 3 "	0	0	0	0	0	0	0	0	0	4	4	4	4	I6	4
Z.O. 3 "	0	0	0	I6	I6	I6	-	-	-	I6	I6	I6	4	I6	64
X.I. 6 "	0	0	0	I6	I6	0	64	256	64	64	I000	256	I6	256	64
K.Ya. 8 "	0	0	0	4	0	0	I6	0	I6	I6	I6	64	I6	64	64
S.Ya. 5 "	0	0	0	4	I6	0	I6	I6	4	4	64	4	4	64	4
A.A. 5 "	0	0	0	4	0	0	4	4	4	4	4	I6	4	4	I6
K.U. 4 "	0	0	0	0	0	0	0	0	0	0	4	4	4	I6	I6
N.N. 2 "	0	0	0	4	4	0	4	4	I6	I6	I6	I6	I6	I6	64

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Table 2 - Antibody response in triple-negative children immunized with live vaccine

Initials and age of children	Before vaccination			4 weeks after feeding with monovaccines									60 days after vaccination		
				Type III			Type I			Type II					
L.N. 2 yr.	0	0	0	4	4	I6	64	64	I6	64	64	I6	64	64	I6
M.T. 2 "	0	0	0	-	-	-	64	I6	I000	I000	4000	4000	I024	4000	4000
R.L. 2 "	0	0	0	I6	I6	I6	64	I6	64	256	I000	I000	I000	4000	256
P.U. 3 "	0	0	0	I6	64	64	64	64	64	256	I000	256	256	I000	256
V.V. 3 "	0	0	0	0	0	I6	-	-	-	64	I000	64	256	256	256
A.A. 2 "	0	0	0	0	4	4	64	64	256	64	I000	256	I000	4000	256
N.N.	0	0	0	4	4	0	4	4	I6	I6	I6	I6	I6	I6	64

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Table 3 - Rate of antibody titer increase in triple-negative children 60 days after immunization

Vaccination schedule	No. of children tested	Age (yr)	No. of children without change in antibody titer			Number of children with indicated increase in antibody titer																	
						4x			16x			64x			256x			1024x			4096x		
			1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
I-III-II	19	3-7	0	0	0	8	1	3	7	5	5	2	6	7	1	4	2	0	2	0	1	1	1
III-I-II	7	2-3	0	0	0	0	0	0	0	0	0	1	1	1	0	2	1	4	3	1	1	1	4	1

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Table 4 - Rate of antibody titer increase in children (with naturally acquired immunity and negative before immunization) 60 days after feeding with live vaccine

Vaccination schedule	No. of children tested	Age (yr.)	No. of children without change in antibody titer	Number of children with indicated increase in antibody titer																	
				4x			16x			64x			256x			1024x			4096x		
				I	2	3	I	2	3	I	2	3	I	2	3	I	2	3	I	2	3
I-II-III	31	0-2	2	9	3	7	6	4	5	4	4	3	2	5	4	4	3	4	3	4	3	3	I	I
III-I-II	11	1-2	0	I	2	I	2	I	I	0	3	3	3	I	3	4	5	4	2	0	0	0	0
I-III-II	37	1-3	I	3	3	9	6	8	9	5	I	0	8	I	0	7	6	II	I	0	4	4	I	2	0	0
I-III-II	35	4-5	9	6	I	3	8	9	9	9	9	9	5	9	2	3	4	0	0	0	0	0	0	0	0
I-III-II	37	6-7	5	4	I	0	II	I	2	II	I	2	7	I	0	7	II	6	2	6	0	0	0	0	0	0

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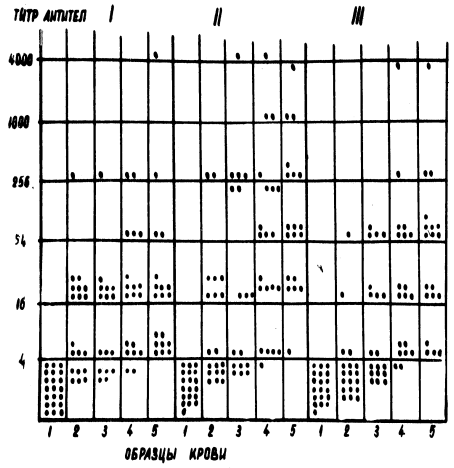

Fig.I - Dynamics of changes in antibody titers in triple-negative children during immunization.

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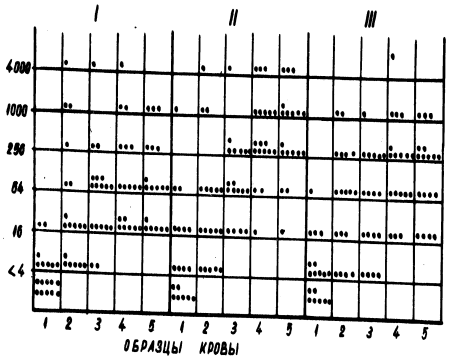

Fig.2 - Dynamics of changes in antibody titers in children of 0 to 3 years of age immunized on the schedule types III-I-II

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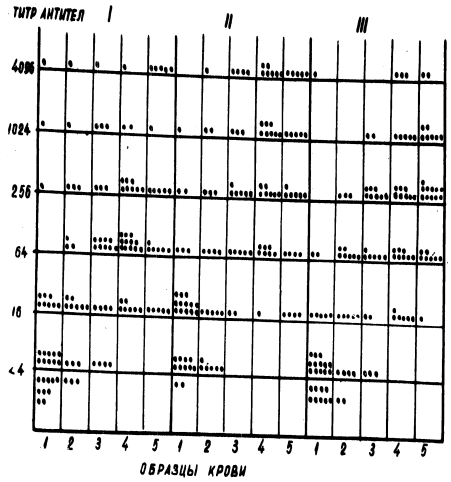

Fig.3 -Dynamics of changes in antibody titers in children of 0 to 3 years of age immunized on the schedule type I- type II-type III

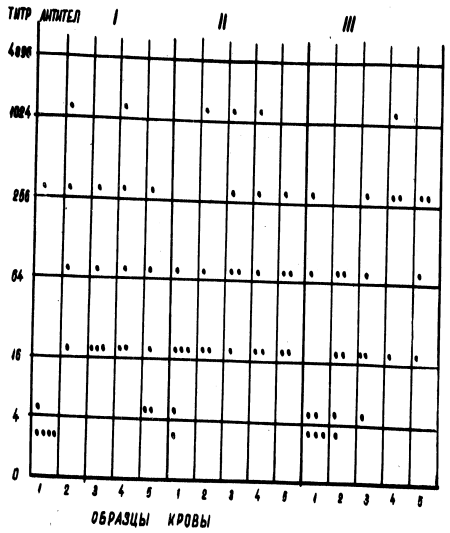

Fig.4 - Dynamics of changes in antibody titers in children of 0 to 3 years of age immunized on the schedule type I; type II ,-typeIII.

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STAT

Problems of manufacture and control of live poliovirus vaccine from A.B. Sabin's attenuated strains

Chumakov, M.P., Dzagurov, S.G., Gagarina, A.V., Lashkevitch, V.A., Ralph, N.M., Mironova, L.L., Shmeleva, G.A., Khanina, M.K., Elbert, L.B., Chernyshev, V.I., Robinson, I.A., Ravkina, L.I., Tsypkin, L.B., Tufanov, A.V.

Moscow

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In December 1958 - February 1959 first lots of live poliovirus vaccine from Sabin's attenuated strains were manufactured at our Institute. This amount was sufficient for triple immunization of 10 million persons. The vaccine has successfully passed all control tests and has additionally tested by the author of the live vaccine, Dr. A.B. Sabin, and was favourably estimated. All lots of the live vaccine of the first manufacture cycle were successfully used for mass immunization of the population in spring and summer, 1959.

Characteristics of these lots of the live poliovirus vaccine were reported at May Conference on live vaccine in Moscow, 1959, and at the International Conference on live vaccine, Washington, June 1959, and also in papers published in the journal "Problems of Virology" and in WHO editions.

Because of sharply growing demands for live poliovirus vaccine we continued its manufacture and developed a new form of the preparation - dragée-vaccine, acquired certain experience both in manufacture and biologic control of the live vaccine which is summerized in this communication.

Main requirements for live vaccine manufacture and control in the USSR are set forth in official instructions approved by the USSR Ministry of Health in November 1959. In development of and addition to these instructions we adopted some more directions given by the author of the live vaccine, Prof. A.B. Sabin, in his letter of August, 1959. It should be said that after the Washington Conference on live vaccine in June 1959, a small group of investigators headed by A.B.

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Sabin discussed at length all the main problems of live vaccine manufacture and control and came to some decisions which were stated in the mentioned letter by Dr. A.B. Sabin and followed in our work.

The question is, first of all, in strict usage of one well-tested seed material (first or second passage from the author's vials) and maintenance of definite temperature of incubation of inoculated tissue cultures (not higher than 34-35 ^{0}C). All this should secure the stability of hereditary properties of attenuated poliovirus vaccine strains and best reproducibility of vaccine virus multiplication.

Furthermore, new additional directions required more stringent tests for the absence of contamination of tissue cultures with spontaneous simian viruses, including B virus, and with mycobacteria tuberculosis.

As is known, in addition to our official instructions for manufacture and control of the live vaccine drawn up mainly after A.B. Sabin's directions, some more suggestions have been made, for example, in Report No. 2 of the American Technological Expert Committee on live poliovirus vaccine headed by Dr. R. Murray. Some of these suggestions were taken into consideration in our practice of live vaccine manufacture and control.

Some of the suggestions by this Committee, however, such as tests of the vaccine for the absence of the capacity to produce viremia in children, neutralization tests with at least 500 ml of the virus from each lot against hyperimmune rabbit-serum, keeping of monkeys for six weeks before sacri-

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fice in individual cages, and others were found to be unaccomplishable regularly in practice and they proved absolutely unnecessary.

Manufacture of the live vaccine at the Experimental-Production Department of our Institute for almost 1 1/2-year period may be divided into 2 production cycles (see Tables). A total of more than 60 lots of the live vaccine has been manufactures both in the form of monovaccines of types I, II and III and trivalent mixture (over 180 individual batches of vaccine virus in total volume of more than 4000 litres, or about 400 million inoculation doses). This amount of the manufactured vaccine was not the limit of our production facilities and could be doubled or tripled if necessary, with comparatively small additional expenses.

This fact clearly indicates that one comparatively small institute, like ours, with experienced personnel can successfully solve the problem of serial production of live vaccine and of regular supply with this preparation for the largest program of mass poliomyelitis immunization ever known in history. Therefore it would be advisable to accept the suggestion in future to concentrate maintenance of seed vaccine strains and manufacture of the live poliovirus vaccine itself in a few regional centers having well-equipped production facilities and highly-trained specialists - virologists. This will ensure complete safety and good quality of the vaccine with strict observance of the established regulations of vaccine manufacture, and rapid supply of the vaccine in necessary amounts to all countries belonging to certain zones.

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At our Institute manufacture of the live vaccine is concentrated in a separate building where no other work with any viral or bacterial preparations is done. Laboratories for vaccine control are housed in another building.

Tissue cultures for vaccine virus propagation are prepared from trypsinized suspensions of monkey rhesus kidney tissue in flat bottles of home production (1 1/2 litre capacity). Medium for cell growth contains 0.5 % lactalbumin hydrolisate in Earle's solution with 2% heated bovine serum, pH 7.5. Uninoculated cells are incubated at 37° C. From 10 to 25 per cent of cultures from each pair of kidneys are kept uninoculated for three weeks with medium change at 7 days to check for the absence of spontaneous degeneration of cultures due to simian viruses.

Cultures grown for 7-8 days, with good dense cell sheet are inoculated with seed virus (each type separately) in doses of about 2000 TCID per 350 ml of medium. Maintenance medium after inoculation of cultures contains no serum (0.5% lactalbumin hydrolysate in Earle's solution with increased content of bicarbonates and glucose). Inoculated cultures are put on pendulous shelves which are slowly swinging on a rocker (up to 30 swingings per hour) and are incubated in a special thermostatic room at 34° C.

After complete degeneration of cultures (during 2-4 days) they are repeatedly frozen and thawed, culture fluid is collected from the bottles, samples for control are taken, and then separatebatches of virus are pooled in vaccine lots of 50 to 200 litres each. All kinds of control tests are at present

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performed simultaneously both for initial small batches of virus, corresponding to separate inoculation of cultures prepared from 1-3 pairs of kidneys, and for pooled lots of vaccine prepared for filtration and after filtration. Such combination of all steps of the control proves completely justified because of comparatively small risk of discarding small volumes of vaccine virus batches. But it saves much time in release of finished vaccine after all control tests have been completed.

During the first cycle of live vaccine manufacture the control was performed step-wise with regard for the results of each previous control test. This led to considerable delay in release of the vaccine.

After pooling in a lot the vaccine is filtered through asbestos filters S_1. Schemes show the main lines of biologic control in live vaccine manufacture.

Control is divided in two main groups: tests in several animal species and tests in tissue cultures (see separate communications by Dzagurov, S.G., and Shmeleva, G.A.).

We attach great importance to preliminary selection of monkeys from which kidneys are removed for tissue cultures. Due to thorough clinical and pathoanatomical examination monkeys with tuberculosis, clinical infection caused by B virus, and other infections are rejected.

Furthermore, parallel observations on control uninoculated kidney tissue cultures helps to discard additionally occasional cultures because of spontaneous degeneration or appearance of filarial parasitizing in monkey blood. Filarial have

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been found on two occasions. This confirms the necessity to retain the stage of vaccine filtration through asbestos filters in order to completely ensure against penetration of filarial into the vaccine. B virus has never been detected during this 1 1/2-year period, probably due to stringent rejection of monkeys at preliminary stages of control, during kidney removal, and due to monthly quarantine for all monkeys before use.

For a long time we carried out biological control of the vaccine from separate small batches of virus before pooling in lots by inoculation of suckling and adult white mice, rabbits, guinea-pigs and so on. Then we found it more advisable to carry out all control tests in animals after pooling separate batches into a lot before filtration. This is fully justified and gives good results by their agreement with control in tissue cultures. At the same time we retain control tests in tissue culture for each separate small batch of virus including tests for t marker, potency, identification, absence of B virus and of other simian viruses. These tests are repeated in tissue cultures for batches pooled in lots before filtration and besides test for virus titer(potency of the vaccine) is done additionally after filtration.

We must admit that the current methods of live poliovirus vaccine control are extremely labour-consuming and complicated. Some simplification of this control is quite possible, provided strict consistency of production technology is observed and most important control stages, such as tests for B virus and for mycobacteria tuberculosis, are retained. In our opinion, the danger of oral vaccine contamination with spontaneous sinian viruses,

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except B virus, is not very great. It is necessary, however, to continue improving methods of tests for spontaneous simian viruses.

Several schemes present kinds of biological control of vaccine used in our Institute, and tables summarize the results of control tests for separate groups in two production cycles, including those lots of vaccine which have passed complete control tests.

A total of 4 lots of vaccine have been discarded (lot No. 30 of type II, and lots No. 26, 29, 32 of type III), and two more lots are undergoing repeated control. With the discarded lots occasional cases of paresis were noted on intracerebral inoculation of monkeys, with all other control tests giving quite satisfactory results. 44 lots of vaccine have completely passed all control tests and have been released for use.

Without discussing at length schemes and tables presented here, it may be said that the system of live vaccine control based on A.B. Sabin's directions accepted in the Soviet Union after long practical trials has proved to be quite satisfactory which is confirmed by good results of use of the live vaccine for mass immunization of people.

A few words should be said of a highly promising preparation of the vaccine in the form of dragée-candy. As will be shown in a number of communications of this Conference dragée-vaccine has been found to be a very convenient form for mass use. It is possible, with the candied vaccine, to carry out immunization on a very large scale in a short time. This saves

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labour spent by local medical workers on distribution of the diluted vaccine and on giving it in drops. Dragée-vaccine is very stable to variations in temperature, namely, at - 20°C it is preserved without loss in titer for about 3 months, at 4°C about one month and at room temperature for at least 3-5 days. Such time is quite sufficient for carrying out mass immunization with the live vaccine in dragée-candy provided population is prepared for vaccination in advance.

Regular repeated tests in different laboratories of the Institute demonstrated quite satisfactory distribution of vaccine virus in individual candies of each lot. As a rule, in tests with individual candies there was variation in titer not more than 0.5 log which is within the standard error in poliovirus titration by current methods.

It should be emphasized that the best reproducible results of titrations are obtained by plague method (after Dulbecco, Hsiung and Melnick).

The candied vaccine is very convenient for moast broad one-time immunization of large masses of population whereas the liquid vaccine, being more compact and allowing for longer storage in small refrigerators, is more convenient for vaccination of small children's communities or for planned vaccinations of growing-up children of younger ages. Accordingly, we continue and in future will enlarge the release of liquid vaccine in vials, side by side with manufacture of dragée-vaccine. It is quite possible to prepare supplies of liqui vaccine in vials instore for several years and to keep it in frozen state until use when demanded.

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Experimental tests of candied live poliovirus vaccine in tissue culture

M.P. Chumakov, A.D. Bezzubov, S.G. Dzagurov, G.A. Shmeleva, L.M. Vilner

(Institute for Poliomyelitis Research, Academy of Medical Sciences, USSR)

In April-July 1959 on Professor M.P. Chumakov's initiative 1 experiments were made for elucidating the possibility of including live poliovirus vaccine into candy mass (Bezzubov, A.D., Fleer, G.P., Chumakov, M.P., 2). Examination of the vaccine titers in mixtures with sugar and candy mass showed good preservation of the virus at certain temperatures (Fleer, G.P., 2). Satisfactory results were obtained in investigations of the establishment and immunogenic activity of candy-vaccine in the vaccinated children (Fleer, G.P., 3 , Voroshilova, M.K., Taranova, G.P. 4).

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In September 1959 the Institute for Poliomyelitis Research of the Academy of Medical Sciences, USSR, together with All-Union Scientific Research Institute of Candy Industry (Professor A.D. Bezzubov) developed Technical Requirements for production of live poliovirus vaccine in the form of dragée-candy.

After these Technical Requirements had been approved by State Sanitary Inspection of the USSR and Technical Department of Moscow City Council of national economy Marat Candy factory started large-scale production of dragée-candies containing mono- or trivalent live poliovirus vaccine.

Each lot of the candied poliovirus vaccine was virologically tested at the Department of biologic control of viral preparations of the Institute for Poliomyelitis Research, AMS, USSR. For the manufacture of dragée live poliovirus vaccine was used from Sabin attenuated poliovirus straines type I - LSc, 2 ab; type II - p 712, CH, 2 ab and type III - Leon, 12a,b, which had passed through all the stages of animal and tissue culture control tests 6 .

In the process of dragée manufacture the vaccine is thoroughly mixed with syrup cooled to 25^{0}C (pH 6.8-7.2) containing 69% sucrose, 8% glucose, 8% fructose, 15% water

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and small amount of food dye. During 1-1.5 hours in roller boiler at a temperature up to +25°C a strictly definite by volume quantity of syrup with the vaccine is evenly distributed, with addition of sugar powder, into approximately 30,000 crystal sugar granules. Then in the same boiler outer sugar-fatty-waxy cover is deposited on the resulting spherical dragée-candies for prevention of their drying up.

The amount of live poliovirus vaccine introduced into candy mass varied in different vaccine lots from 50,000 to 350,000 TCD of virus per one dragée-candy weighing 1 gm, and on the average was about 100,000 TCD.

The technology of dragée manufacture in roller boilers allows ± 15% variations in the weight of individual candies which is of no great significance for vaccine dosage because of considerable excess of the amount of cultural units of the vaccine virus introduced into candies (according to experimental data of a number of investigators, a minimal immunizing dose of the live vaccine is about 10,000 TCD of poliovirus).

The whole process of manufacture of dragée-candy with the vaccine (including packing in parcels) goes on at room temperature not higher than 25°C and is over in 3-4 hours.

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The finished dragée with the vaccine is stored until shipment to consumers at -20°C. During transportation of dragée-vaccine (mainly by air) and until use for immunization it is allowed to keep the kandy at room temperature not longer than for 3-7 days, and at +4°C not longer than 1 month.

The present paper describes the results of titrations of the candied live poliovirus vaccine and the results of tests for virus preservation in candy at different temperatures and after different periods of storage.

Methods.- The candied poliovirus vaccine was titrated by the plague method [7] modified by Hsiung and Melnick [8].

Dragée-candies (average weight of 1 piece - 1 gm) were dissolved in medium 199, containing penicillin and streptamycin, 1000 units per ml, each. Dilutions of dragée from 1 = 200 to 1:750 were prepared in this medium. 0.1 to 0.2 ml of each dilution was added in each of 2-3 bottles with 7-day culture of trypsimized rhesus monkey kidney cells (the surface of cell monolayer = 60 cm^2). Inoculated cultures were kept for 1 hour at + 37°C, layered with agar and then again incubated at +37°C. The results were read at 5 days.

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Results

In the first stage of the work titrations were made with experimental samples of candied vaccine manufactured in small amounts. The findings indicated that from 70.9 to 94.3% PFU of live poliovirus vaccine was preserved in the process of dragée manufacture which confirmed the acceptability of technology for candied vaccine manufacture at Marat factory.

Subsequently in process of production manufacturing of the candied vaccine at the factory loss of the virus was found to be negligible.

According to technical conditions for manufacture of the live poliovirus vaccine in the form of dragée-candy each candy is allowed to contain 100,000 $\pm$ 50% of virus particles. In connection with this for production manufacturing of the candied vaccine such doses of the live vaccine were selected which provided for sufficient content of virus particles in dragée-candies. This is shown by the results of titrations done for control of production lots of the candied vaccine presented in Table 1.

It may be seen from the data in Table 1 that when a liquid monovaccine was used one dragée-candy contained at

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least 70,000 (7×10^4) plague-forming units, and with trivaccine one dragée contained over 227,000 (2.27×10^5) PFU.

In the process of manufacturing large lots of the candied vaccine not less than 83.8% PFU was preserved, as a rule, in one dragée-candy.

Table 2 presents the results of investigations on eveness of distribution of virus particles in dragée from one batch of the candied vaccine. For this experiment dragée were taken from different boxes with the finished vaccine.

The data in Table 2 show that the virus distribution to individual dragée is sufficiently even. (The ratio showing variation of the virus content in dragée is 17.4%, and the doubled error of arithmetic mean is $\pm$ 16,200).

Tables 3 and 4 present results of titrations of the candied live vaccine after various periods of storage at different temperatures.

These data indicate that the storage of the candied vaccine at sub-zero (-20° C) and refrigerator ($+4^{\circ}$ C) temperatures does not cause any significant losses of virus particles in dragée.

When the candied live vaccine is stored at room temperature for 10 days or longer the number of plague-forming units in dragée is reduced by 50 per cent or more.

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Conclusions

1. The technology of manufacture of the candied live poliovirus vaccine makes it possible to produce candies with any amount of virus particles necessary for immunization, in one dragée.

2. The candied live poliovirus vaccine stands storage at +4°C and - 20°C.

3. Storage of the candied poliovirus vaccine at room temperature for periods longer than 10 days causes significant loss of the virus in dragée. The decline in titer begins already 3-5 days after storage at room temperature. Therefore it is recommended to store the dragée-vaccine at room temperature for periods not longer than 3-5 days.

References

1. Chumakov, M.P., Voroshilova, M.K., Drozdov, S.G., Dzagurov, S.G. and others - "On mass oral immunization of population in the Soviet Union against poliomyelitis with live vaccine from A.B. Sabin's attenuated strains", published by the Institute for Poliomyelitis Research, AMS, USSR, pp.1-77, Moscow, 1960.

2. Bezzubov, A.D., Fleer, G.P., Chumakov, M.P. - Experimental data on the possibility of including live polio-

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

virus vaccine into candy. Proceedings of the IV-th Conference of the Institute for Poliomyelitis Research, AMS, USSR, May 17-20, 1960. Manuscript.

3. Fleer, G.P. Virologic and serologic evidence of immunization of children with candy containing live poliovirus vaccine.- Ibid, May 17-20, 1960.

4. Voroshilova, M.K., Taranova, G.P.- Unpublished data.

5. Sabin, A.B.- F J.Am.Med. Assn. 1956, 162:1581,

Ibid, 1957, 164:1216.

Brit.Med. J. 1959, 1:663.

6. Chumakov, M.P. and others.- Problems of Virology,1959:529.

7. Dulbecco, R. & Vogt, M.- Ann. N.Y. Acad. Sci.,1955,61:791

8. Hsiung, G.D. & Melnick J. - J.Immunol.1957,78:128; 1958, 80:282

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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Table 1

Results of control titrations of production lots of the candied live poliovirus vaccine

Date of dragée manufacture	Date of titration	t° and period of storage	number of PFU in vaccine given per 1000 dragée candies (1 kg)	Estimated number of PFU per 1 dragée by titration	Number of PFU per 1 dragée by titration	Ratio of actual to estimated number of PFU per 1 dragée	Virus type and lot number
12.I.1960	6.I. 1960	-20°C 3 days	89.13×10^6	89×10^3	88.75×10^3	99.5%	I; N.25
15.I.1960	16.I. 1960	-20°C 1 day	241.85×10^6	242×10^3	227.188×10^3	93.9%	I, II, III, Nos. 25, 31, 28
1.II.1960	5.II. 1960	-20°C 3 days	12.5×10^6	125×10^3	120.625×10^3	96.5%	III; No. 34
3.II.1960	5.II. 1960	-20°C 1 day	250×10^6	250×10^3	$216,563 \times 10^3$	86.6%	III; No. 34
4.II.1960	5.II. 1960	-20°C 12 hrs.	60.26×10^6	60×10^3	70×10^3	116%	I; No. 23
10.II. 1960	11.II 1960	-20°C 12 hrs.	79.62×10^6	79×10^3	79.375×10^3	99.7%	I; No. 35
17.II. 1960	16.III 1960	-20°C 26 days	$141,58 \times 10^6$	142×10^3	124.375×10^3	87.7%	III; No. 34
25.II. 1960	9.III 1960	- 20°C 12 days	87.1×10^6	87×10^3	83.75×10^3	93.8%	I; No. 25
29.II. 1960	25.III 1960	- 20°C	174.2×10^6	174×10^3	170.625×10^3	90.8%	I; No. 25

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Table 2

Distribution of virus particles in the candied live poliovirus vaccine

Virus type in dragée	Vaccine lot number	Number of PFU in vaccine given per 1000 dragée candies	Dragée number	Number of plagues in bottles Bottle 1	Bottle 2	Bottle 3	Number of PFU in 1 dragée candy	Average number of PFU in 1 dragée candy (M)	Mean square deviation (σ)	Doubled error of arithmetic mean (2xSD)	Variation ratio (V)
			1	124	131	121	125×10^3				
			2	144	124	160	143×10^3				
			3	134	174	148	152×10^3				
			4	180	187	194	187×10^3				
I, II, III	Trivaccine No. 21	162.69×10^6	5	178	138	164	160×10^3	147×10^3	25.6×10^3	$\pm 16.2 \cdot 10^3$	17.4%
			6	160	137	194	130×10^3				
		Estimated number of PFU in 1 dragée candy = 162×10^3	7	209	148	194	184×10^3				
			8	133	163	179	158×10^3				
			9	128	130	115	124×10^3				
			10	113	109	110	111×10^3				

Notes:

1) 0.1 ml of $10^{-2.0}$ dilution of dragée was added to each bottle

2) σ - mean square deviation

M - average number of PFU in 1 dragée-candy

V - variation ratio $\frac{\sigma}{M} \times 100\ \%$

3) 2·SD = doubled error of arithmetic mean

4) $SD = \frac{\sigma}{\sqrt{n}}$; n - number of observations .

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Table 3

Preservation of the virus in the candied live poliovirus vaccine at different temperatures

Virus type in dragée	Conditions of storage	Period of storage (days)	Number of PFU in 1 dragée-candy	Ratio of number of PFU to control %
I	+18°+22°C (in the room)	3	72.5×10^3	96.6%
		5	44.375×10^3	59.2%
Lot No. 25	+ 4°C (in refrigerator)	3	78.125×10^3	104.1%
		5	65×10^3	86.6%
	-20°C (control)	10	75×10^3	100 %
	+18°+22°C (in the room)	10	34.375×10^3	19.8%
I	+4°C (in refrigerator)	10	161.25×10^3	92.6%
Lot No. 25	-20°C (control)	15	173.125×10^3	100 %
I	+18°+22°C (in the room)	15	33.125×10^3	20.2%
Lot No. 23	+4°C (in refrigerator)	15	96.825×10^3	83.7%
	-20°C (control)	30	114.375×10^3	100 %
	+18°+22°C (in the room)	15	13.125×10^3	18.7%
II Lot No. 31	+4°C (in refrigerator)	15	73.125×10^3	100.4%
	-20°C (control)	30	70×10^3	100 %
III Lot No.34	+18+22°C (in the room)	15	47.5×10^3	37.2 %
	+4°C (in refrigerator)	15	136.875×10^3	107.3 %
	- 20°C (control)	30	127.5×10^3	100 %

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Table 4

Preservation of the virus in the candied live poliovirus vaccine at subzero temperature (-20 °C)

(Experimental lots)

Date of dragée manufacture	Virus type	Date of titration	Period of storage (days)	Number of PFU in the vaccine given per 1000 dragée-candies (1 kg.)	Estimated number of PFU in 1 dragée-candy	Number of PFU in 1 dragée candy by titration
3.XI.59	III	9.III.1960	125	53.4×10^6	53.4×10^3	60×10^3
4.XI.59	III	9.III.1690	124	53.4×10^6	53.4×10^3	52.5×10^3
18.XI.59	II	18.III.1960	91	37.77×10^6	37.77×10^3	31.9×10^3

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ACADEMY OF MEDICAL SCIENCES OF THE USSR

INSTITUTE FOR POLIOMYELITIS RESEARCH

STAT

THE STUDY OF GENETIC SIGNS STABILITY OF POLIOVIRUS STRAINS ATTENUATED BY A.SABIN

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Of late live poliovaccine is becoming an object of ever increasing attention on the part of investigators and medical workers in the field. To prepare it a series of poliovirus strains have been proposed (Sabin,1957,1959=a,Koprovsky,1958, Cabasso, Cokes and oth.,1959, Ezersky,1959). The widest recognition,however, received live poliovirus vaccine prepared from the strains attenuated by A.Sabin (Smorodintsev with coll.,1959,Chumakov wt with coll,1959, Shkovranek with coll,1959, Hale with coll,1959, Alvarez with coll.,1959 and others).

By a number of genetic signs the strains attenuated by Sabin distinguish themselves qualitatively from virulent strains. Amongst these most essential are: their non=pathogenecity for monkeys in intracerebral infection- N signs (Sabin,1957,1959a), relative uniformity of the plaques size and shape with their smaller dimensions- S sign (Sabin,1955), incapacity to multiply with the acid pH- d sign (Vogt, Dalbecco,Wenner,1957, Dalbecco, Vogt,1958, Hsiung,Melnick,1958), and also at 40°C -T sign (Lvov, 1959,Sabin,1959b). Genetic signs of the strains used in vaccination are to be sufficiently stable(Ginsburg,1947,1959).

The purpose of the present work was to study the stability of genetic signs in poliovirus strains attenuated by Sabin, both in the course of laboratory passages and during their propagation in the intestine of vaccinated children.

MATERIALS AND PROCEDURES.

Virus. As objects of experijents served the follwoing poliovirus strains, attenuated by Sabin: the strain of the I type LSc, 2ab,type II strain P-712,Ch,2 ab,type III,Leon,12 a_1b In control experiments were employed the following virulent poliovirus strains: type I strains of Mahoni and Brunden,type II strains MEF_1, type III Sockett strain. In addition to this investigated

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were also a number of natural poliovirus strains isolated from the feces of clinically healthy children and those isolated from the excreta of children immunized with live poliovirus vaccine.

Tissue Culture. In all the experiments were used tissue culture of the Macaca=rhesus kidneys. Trypsinized cells were cultured on a medium comprised of a 0.5% lactalbumin hydrolysate in Hanks solution with 2% calf serum. Before inoculating the cells the culture medium was replaced with the medium 199,containing no serum, with pH amounting to 7.4-7.6.

Monkeys. Monkeys of the Macaca=rhesus genus were taken, weighing 2-3 kg, whose blood serum was devoid of inhibitors to any of the three types of poliovirus.

Titration of the virus. Dilution of the virus was effected with and interval of 0.5lg. Each virus dilution was used to inoculate 4 test tubes containing the tissue culture, in the amount of 0.1 ml per each test tubel The testing of infected cultures was made on the 7th day.

Method employed to Inoculate monkeys. A/B-spinal cord of the monkeys: The investigated virus was introduced in the amount of 0.5 ml into the gray matter of the lumbar enlargement of the monkeys with a needle No 20, in conformity with the procedure recommended by Sabin (1959a).B/C.Cerebrum: 0.5 ml of the virus under investigation was administered into the region of the right=hand thalamus with a needle No 24 in strict conformity with the procedure proposed by Sabin (1959a). When studying the initial attenuated strains the virus in amounts of 0.5 ml was being introduced into the both thalamuses.

Monkeys were kept under observation for 21 days,folloing which the animals were sacrificed and prtions of their central nervous system were taken for subsequent morphological and

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virusological examination. Clinical diagnosis of a specific paralysis or paresis were made only when this could be confirmed by morphological changes in the central nervous system.

Procedure adopted to isolate the virus from the feces.

A 20% suspension of the feces was centrifuged at 6000 revolutions per minute for one hour. Upon the addition of antibiotics (penicillin and streptomycin) the supernatant liquid was placed in a refrigirator at a temperature of -20°C. On its defrosting portions of 0.2 ml. of the supernatant fluid were introduced into each of the 5 test tubes containing the tissue culture. The infected cultures were kept under observation for 10 days. The specificty of cell degeneration was tested by special passages and typing.

Methods employed in morphological investigations of the central nervous system. Pieces of the spinal cord and cerebrum were fixated in a 10% solution of neutral formalin. Investigations involved the the motor area of the cortex in the region of the precentral convolution, frontal sections on the level of the thalamus, three levels of the brain stem, spinal cord on the levels C_4, C_6, C_8, Th_6, L_2-L_5. Paraffin slices were stained with hematoxilin and eosin and with thionin after Nissle.

Methods used in the study of the plaques size and shape. The plaques size and shape were studied by the methods suggested by Hsiung and Melnick (1957). Plaques estimation was made on the 5th day. Average plaques sizes and variations thereof were determined by measuring 100 plaques of each strain under investigation.

Methods employed for the study of the virus multiplication under different pH. The virus propagation beneath agar under varying sodium carbonate concentrations (pH) was studied by the Hsiung and Melnick(1958) procedure.

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Methods used to study the virus multiplication under different temperatures. A somewhat modified procedure, described by Lwoff (1958,1959) was employed. In the culture comprised of the monkey renal tissue, grown at 36°C, the culture medium was replaced by the medium 199 with pH equal to 7.6-7.8. Infection was effected on the next day. All the test tubes with infected cultures were kept for 30 minutes at 30°C, following which that portion of inoculated cultures which had to be kept at 40°C would be transferred into corresponding thermostat. Infected test tubes were incubated in small=sized laboratory thermostats supplied with a water=cooling jacket. As indicated by supplementary recording devices, placed inside the thermostats, temperature fluctuations did not exceed 0.3°C. The examination of inoculated cultures was effected on the 7th day.

Techniques employed in identification of individual strains of the same type. To identify poliovirus strains of the same type a somewhat modified technique, described by Mc Bride was used..The value of K was determined on the basis of formula, given by Mc Bride: $K = 2.3bg\frac{Y_0}{Y_t}$, where K= is the neutralization rate, D -1) anteserum dilution, Y_0 and Y_t - virus activity at the moments 0 and t.

R E S U L T S.

The task of the first set of investigations was to study genetic signs of the poliovirus strains attenuated by Sabin.

From the original poliovirus strains obtained from Sabin small batches of each virus type were prepared in strict conformity with the recommendations put forward by Sabin. This was done at the Moscow Institute of virus preparations. Upon successful

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completion of all control operations, the virus thus obtained was poured off into individual ampoules and kept there at -45°C.

Table 1 lists data representative of the study relative to the neurotrotropismof attenuated poliovirus strains consequent upon their intracerebral inoculation to monkeys (N-sign).

T a b l e 1.

Neurotropic study of attenuated poliovirus strains in monkeys subject to intracerebral infection.

Virus	The dose introduced (Lg.TCPD-50/ml)	Manifestations of the disease		
		Clinical	Morphological	
			only in the Thalamus region	spread outside the thalamus region
Type I strain LSc,2 ab	7.5	0/10	6/10	2/10
Type II strain P-712,Ch,2 ab	6.5	0/10	0/10	0/10
Type III strain Leon,12,a_1b	7.8	0/10	0/10	0/10

From the figures cited in table I one can see that intracerebral infection of monkeys with the poliovirus strains under investigation failed to produce any clinical manifestations of this disease. As a rule, morphological alterations either were completely absent, or were due to the administration technique, and in this latter case they were manifest, mainly, in the development of massive histocytic=lymphoid cuffings, without any lesion of the neurons, worth of speaking. These lesions can hardly be unreservedly attribued to poliomyelitis.(Fig.1). In was only in two instances that there were specific morphological

Fig. 1.

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changes, which were marked beyond the thalamus region, spreading in one monkey as far as the mid=brain, and in another- to the lumbar enlargement. The degree of these lesions,however, was very insignificant.

Hence, in the initial attenuated poliovirus atrains the N-sign,i.e. the steeply reduced pathogenicity in monkeys subject to intracerebral infection, was pronounced quite distinctly.

As already stated above markedly low pathogenicity peculiar to the the attenuated poliovirus strains has been also revealed in monkeys inoculated into the spinal cord. Table 2 includes some data relative to the study of neurotropic properties of the virus in monkeys infected into the spinal cord.

Table 2.

The study of neurotropism specific to the poliovirus strains in attenuated by Sabin monkeys infected into the spinal cord.

Virus	The dose introduced (lg TCPD50/ml	Clinical	Morphological	
			in the region of the lumbar enlargement only	spread beyond the lumbar enlargement
Type I strain LSc, 2 ab	0.5.7.5	2/12	6/12	4/12
	0.5.6.5	1/6	3/6	2/6
	0.5.5.5	0/5	4/5	0/5
	0.5.4.5	0/6	2/6	0/6
Type II strain P-712,cb, 2 ab	0.5.6.5	0/12	5/12	0/12
	0.5.5.5	0/6	3/6	0/6
	0.5.4.5	0/6	1/6	0/6
	0.5.3.5	0/6	0/6	0/6
Type III strain , Leon,12- a_1b	0.5.7.8	0/12	5/12	3/12
	0.5.6.8	0/6	3/6	1/6
	0.5.5.8	0/6	0/6	0/6
	0.5.4.8	0/6	0/6	0/6

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Data in table 2 are illustrative of an extremely rare incidence of clinical manifestations in monkeys inoculated into the spinal cord with attenuated poliovirus strains. They occurred only in three monkeys infected with the typeI virus, indiluted, or in dilution of 10^{-1}.

Morphological manifestations of poliomyelitis were of a rare frequent occurrence. In most instances morphological alterations specific of poliomyelitis were restricted to the lumbar enlargement of the spinal cord, not infrequently immediately around the site of the virus introdution. In this area,viz; at the very site of the virus injection, morphological changes ordinarily had no difference from those observed during ino-

Fig. 2. culation of virulent virus strains (Fig.2). But already in the spinal segments adjacent to the site of injection the foremost was not the lesion of the anterior horns motor neurons, but , predominantly,alterations of blood vessels,taking the shape of capillary overfilling, histiocytous-lymphoid infiltrates around capillaries and minute arteries; noticeable was also proliferation

Fig. 3. of microglia and oligodendroglise, etc.(Fig.3).

In a number of monkeys, including the animals showing clinical manifestations of the disease, morphological changes went beyond the limits of the lumber enlargement. These changes were met with, chiefly, in the cervical enlargement , in the medulla oblongata and in the motor area of the cortex. The lesion of these divisions was of a rather slight nature and manifested , mainly, in the appearance of productive vasculites with perivascular infiltrates and it was merely in some few places were small histiocytous infiltrates could be found with neurons in

Fig. 4. a fully intact condition.(Fig.4).

A comparison of the results obtained by us following the

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study of morphological changes in the central nervous system of monkeys infected with attenuated poliovirus strains with those known from literature sources and associated with the inoculation to monkeys of virulent poliovirus strains (Bodina, 1948, Robinson, 1957) even in minimal amounts (Gendon with col., 1960) reveals the presence of a singular morphological picture peculiar to the introduction of attenuated Sabin strains. These latter differ from the picture characterizing morphological lesions due to virulent strains not only quantitatively, but also qualitatively. In the main they have two principal features: 1) In the vast majority of cases such morphological alterations are restricted to the site of the virus introduction. When they spread beyond the site of the virus introduction the degree of alterations occurring in these outside areas is relatively indignificant. ") Morphological changes manifest themselves in moderetaly pronounced lesions of nervous cells, including motoneurons, with considerable vascular reaction.

Basing upon the data received we believe that to the already known distinctive features of the attenuated virus strains, distinguishing them from virulent strains (N,S,d and T signs), there may be also added the M sign, reflecting the pathomorphological preculiarities of poliovirus strains attenuated by Sabin.

It is to be noted that it was but on very rare occasions when the attempts to isolate poliovirus from the spinal cord and cerebrum of infected monkeys could give positive results. Thus , from the cord of monkeys sacrificed on the 21st day virus was isolated only in two of the animals, inoculated into the spinal cord, despite the fact that morphological changes witnessing the development of the infectious process could be marked in a considerably larger number of animals. There was not a single case

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of the virus being isolated from the cerebrum.

These results differ substantially from the data on the virus isolation from the central nervous system of monkeys infected with virulent poliovirus strains(Gendon with coll., 1960).

Analogous results with respect to the virus isolation from the central nervous system of monkeys inoculated with attenuated poliovirus strains were obtained also by Marie with coll., 1960).

We staged a number of experiments to study the S,d and T signs of attenuated poliovirus strains the results of which are listed in table 3.

Table 3.

The study of the S,d and T signs of poliovirus strains attenuated by Sabin.

The nature of the virus	Strain	The size of plaques in mm(S sign	Virus propagation wiht different pH(d sign) (lg PFU/ml)			Propagation at different temperature levels(T sign) (lg TPCD50/ml)	
			0.1% soda	0.4% soda	TR	36°	40°
attenuated	Type I,LSc, 2 ab	4.7± 1.14	4.8	7.2	2.4	7.3	1.0
	Type II,P-712,Ch,2 ab	4.6± 1.03	4.3	6.3	2.0	6.6	1.0
	Type III, Leon,12,a,b	5.2± 2.81	5.5	7.8	2.3	7.5	1.0
virulent	Type I Macheni	7.9± 3.32	7.3	7.4	0.1	7.2	7.0
	Type II, MEF_1	7.0± 3.76	6.9	6.9	0.0	7.7	7.7
	Type III Sockett	7.7± 4.01	7.0	7.2	0.2	7.1	7.0

PFU - number of plaque-forming units

TR - ration betwee the virus titers with acid and alkaline pH.

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As seen from table 3 the attenuated poliovirus strains failed to multiply at 40°C (T sign), propagated at a considerably lower level with acid pH (d sign), while the size of their plaques was somewhat smaller and, as contrasted to the virulent strains, its variations were more limited (S sign).

Thus the above investigations of the sum=total of genetic signs (N,M,T and S) demonstrated a clear=cut distinction between the poliovirus strains attenuated by Sabin and virulent poliovirus strains, which is in full accord with the data available in literature sources.

The task of the next set of investigations included the study of genetic signs stability specific to attenuated poliovirus strains, carried out both during laboratory passages and in the course of actual vaccinations of children.

In the first series of these experiments we aimed at studying the stability of genetic properties particular to attenuated Sabin strains in the course of passages at 38°C and 40°CTest tubes with the tissue culture of the monkey kidney containing 1ml. of the medium 199 were inoculated with 1 ml of the attenuated virus and then incubated at 38°C or 40°C. The successive passages were effected at the moment of the maximally developed cytopathogenic action. In cultures were such action was absent- passages were made on the 7th day of the incubation period. A total of 10 passages were effected. After each passage the virus content was determined by means of comparative titration,with the temperature of the passage equalling 36°C.Tables 4 and 5 are illustrative of the virus multiplication in the course of passages at 38°C and 40°C.

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of the virus being isolated from the cerebrum.

These results differ substantially from the data on the virus isolation from the central nervous system of monkeys infected with virulent poliovirus strains(Gendon with coll., 1960).

Analogous results with respect to the virus isolation from the central nervous system of monkeys inoculated with attenuated poliovirus strains were obtained also by Marie with coll., 1960).

We staged a number of experiments to study the S,d and T signs of attenuated poliovirus strains the results of which are listed in table 3.

Table 3.

The study of the S,d and T signs of poliovirus strains attenuated by Sabin.

The nature of the virus	Strain	The size of plaques in mm(S sign)	Virus propagation wiht different pH(d sign) (lg PFU/ml)			Propagation at different temperature levels(T sign) (lg TPCD50/ml)	
			0.1% soda	0.4% soda	TR	36^0	40^0
attenuated	Type I,LSc, 2 ab	4.7± 1.14	4.8	7.2	2.4	7.3	1.0
	Type II,P-712,Ch,2 ab	4.6± 1.03	4.3	6.3	2.0	6.6	1.0
	Type III, Leon,12,a,b	5.2± 2.81	5.5	7.8	2.3	7.5	1.0
virulent	Type I Mahoni	7.9± 3.32	7.3	7.4	0.1	7.2	7.0
	Type II, MEF_1	7.0± 3.76	6.9	6.9	0.0	7.7	7.7
	Type III Sockett	7.7± 4.01	7.0	7.2	0.2	7.1	7.0

PFU - number of plaque-forming units

TR - ration betwee the virus titers with acid and alkaline pH.

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As seen from table 3 the attenuated poliovirus strains failed to multiply at 40°C (T sign), propagated at a considerably lower level with acid pH (d sign), while the size of their plaques was somewhat smaller and, as contrasted to the virulent strains, its variations were more limited (S sign).

Thus the above investigations of the sum=total of genetic signs (N,M,T and S) demonstrated a clear=cut distinction between the poliovirus strains attenuated by Sabin and virulent poliovirus strains, which is in full accord with the data available in literature sources.

The task of the next set of investigations included the study of genetic signs stability specific to attenuated poliovirus strains, carried out both during laboratory passages and in the course of actual vaccinations of children.

In the first series of these experiments we aimed at studying the stability of genetic properties particular to attenuated Sabin strains in the course of passages at 38°C and 40°CTest tubes with the tissue culture of the monkey kidney containing 1ml. of the medium 199 were inoculated with 1 ml of the attenuated virus and then incubated at 38°C or 40°C. The successive passages were effected at the moment of the maximally developed cytopathogenic action. In cultures were such action was absent- passages were made on the 7th day of the incubation period. A total of 10 passages were effected. After each passage the virus content was determined by means of comparative titration,with the temperature of the passage equalling 36°C.Tables 4 and 5 are illustrative of the virus multiplication in the course of passages at 38°C and 40°C.

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Table 4.

Multiplication of poliovirus strains attenuated by Sabin in the course of passages at 38°C.

Strain \ Passages.	The virus titre at 38°C (lg.TCPD50/ml)									
	1	2	3	4	5	6	7	8	9	10
LSc,2 ab	5.1	5.7	6.2	6.0	5.0	4.6	5.3	5.7	5.2	5.9
P-712,Ch,2 ab . .	3.6	3.8	4.5	3.1	2.7	2.6	2.7	3.4	2.8	2.7
Leon,12 a_1b . .	6.1	6.2	6.5	6.6	6.1	5.3	6.0	5.8	6.3	6.0

continued

Strain \ Passage	The virus titre at 36°C (lg.TCPD50/ml)									
	1	2	3	4	5	6	7	8	9	10
LSc, 2 ab	5.1	5.2	6.0	6.4	5.8	4.5	5.2	5.8	5.3	5.7
P-712,Ch.,1 ab . .	4.1	5.2	5.6	5.7	5.6	4.2	4.1	5.6	4.1	4.9
Leon,12 a_1b	5.6	6.3	6.6	6.1	6.5	5.6	5.7	5.9	6.0	6.3

Table 5.

Multiplication of poliovirus strains attenuated by Sabin in the course of passages at 40°C.

Strain \ Passage	The virus titre at 40°C (lg.TCPD50/ml)									
	1	2	3	4	5	6	7	8	9	10
Lsc, 2 ab. . .	≠10	≠10	1.0	1.0	1.0	1.0	-	-	-	-
P-712,Ch,2 ab. .	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Leon,12 a_1b . .	1.0	3.5	3.4	3.6	3.2	4.7	4.6	4.1	4.3	4.2

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Table 5 -continued

Strain	Passage : The virus titre at 36°C (lg.TCPD50/ml)									
	1	2	3	4	5	6	7	8	9	10
LSc,2 ab. . . .	5.0	3.6	1.0	1.0	1.0	1.0	-	-	-	-
P-712,Ch.2ab	3.6	2.7	3.0	3.6	3.5	1.5	1.0	1.0	1.0	1.0
Leon,12 a_1b . .	6.6	5.3	4.5	5.4	4.9	4.6	5.1	4.3	4.7	4.4

From the figures in tables 4 and 5 one can see that in the course of passages of attenuated poliovirus strains effected at 38°C all the three types of the virus were apt to propagate starting from the 1 passage. The titres of the virus,however, and particularly that of the type II, were lower than those, which we were able to observe when cultivating the virus at 36°C.In running the virus through passages at 38°C there could not be seen any notable change in the titre. While making comparative titrations of the virus subject to the passage at 36°C and 38°C, the titres of the types I and III of the virus proved approximately equalThe titre of the type II virus was somewhat higher than at 36°C. During its passages at 40°C the type I strain failed to bring forth any cytopathogenic changes in the cells and in subsequent titration at 40°C could not be detected at all. But titration of the cultural fluid of the first passages at 36°C showed the presence in it of the virus in titre $10^{-5.0}$, in the first passage and in $10^{-3.5}$- in the second. Beginning from the third passage the virus could not be disclosed even at 36°C.

When passaged at 40°C the type II virus did not produce cytopathogenic cellular changes in any one of the passages. However, was when titrating material run through the passage at 36°C the virus could be revealed up to the 6th passage, inclusive.

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All this indicates that in,spite of the absence of cytopathogenic cellular changes during cultivation of poliovirus strains attenuated by Sabin, the virus still multiplies in the cells at 40°C, though at a rate progressively diminishing from one passage to another. The fact that during these experiments there actually occurred propagation of the virus at 40°C without any visible cytopathogenic action and not simple preservation of the residual viruses,introduced while inoculating the cells, is proved, first- by a sufficiently long period of the typeII virus multiplication (in the course of 6 passages), and secondly- by the results of the thermostability studies of the poliovirus strains attenuated by Sabing at 40°C. As a result of tzese experiments we succeeded in disclosing that during incubation at 40°C attenuated poliovirus strains of all the three types become subject to a rapid distruction and in the space of 7 days their titre declines by 5.0-5.5 lograrithmic units.

The type III strain propagated at 40°C exercising visible cytopathogenic action already beginning from the second passage. From the 6th passage onward the virus titre became somewhat higher and equalled that obtained at 36°C.

Genetic signs were studied in the viruses run through 4 and 10 passages. The results of these experiments are represented in table 6 (The study of neuropathogenecity of the type I virus, run through 4 passages, and of the type II one, run through 10 passages at 40°C was carried out with the purpose of detecting the virus, which failed to exercise any cytopathogenic action).

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Table 6.

Genetic signs of poliovirus strains attenuated by Sabin and and run through 4 and 10 passages at 38° and 40°C.

T° of passages	Virus strain	NN of pas	Clin. manif. of poliom. with i.c. infec. monk. (N sign	Morpholog. changes of CNS (N sign): atten. virus type	Morpholog. changes of CNS (N sign): viru. vir. type	Multiplic. at dif. t° (T sign) lgTCPD50/ml: 36°	Multiplic. at dif. t° (T sign) lgTCPD50/ml: 40°	Multipl. with dif. pH (dsign (PFU/ml): 0.1% soda	Multipl. with dif. pH (dsign (PFU/ml): 0.4% soda	Plaque size in mm (S sign)
38°C	Type I	4	0/4	1/4	0/4	6.1	1.0	3.2	5.8	4.6± 1.1.
	LSc,2ab	10	0/4	1/4	0/4	5.2	1.0	2.9	5.1	4.6± 1.1
	Type II	4	0/4	0/4	-	5.7	1.0	3.6	5.7	4.5± 1.0
	P-712, 2ab	10	0/4	0/4	-	4.6	1.0	4.4	4.4	4.7± 1.2
	Type III	4	0/4	0/4	-	6.2	2.0	4.9	6.1	5.3± 2.8
	Leon,12 a_1b	10	0/4	0/4	-	6.2	3.0	5.8	6.0	5.8± 2.9
40°	Type I									
	LSc,2ab	4	0/4	0/4	-	1.0	1.0	-	-	-
	Type II	4	0/4	0/4	-	3.6	1.0	1.1	3.3	4.8 ± 1.2
	P-712 2ab	10	0/4	0/4	-	1.0	1.0	-	-	-
	Type III	4	0/4	1/4	0/4	5.4	3.2	4.4	5.7	6.9± 3.2
	Leon 12 a_1b	10	2/4	0/4	2/4	4.5	4.3	4.4	4.8	7.5± 3.8

The data of table 6 indicate that the types II and I of the attenuated poliovirus strains, run through 4 and 10 passages at 38°C have preserved in full genetic signs of the initial strains (N,M,T,d and S signs.)

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Upon the 4th passage the type III strain showed certain changes in the T and d signs , but even after the 10th passage its neurotropic properties remained unaltered.

From among the strains passaged at 40° active propagation could be obtained only in the instance of the type III. This strain , after the 4th passage, by its T and d signs approached the virulent virus, but retained its N and M signs without any change. Following the 10th passage the type III strain lost all its genetic signs characteristic of attenuated viruses.

The succeeding part of the investigation was devoted to the study of changes in the genetic signs of poliovirus strains attenuated by Sabin during their passage in the spinal cord of monkeys. Monkeys of the Macaca=rhesus genus were inoculated into the cord with 0.5 ml of the virus (2 monkeys for each of the virus type). The animals were sacrificed on the 6th day and thereafter their cord was extracted and from its lumbar enlargment a 20% suspension was prepared. This was then subject to a successive freezing and defrosting and thereafter was used to inoculate test tubes containing monkey renal tissues.Virus isolation was effected simultaneously at 36° and 40°C. Inoculated cultures were kept under observation for 10 days. The isolated virus was then typed, and, after obtaining due confirmation of its being similar to the type of virus employed in inoculating the culture, it was run through the next passage. This latter was done with the aid of a mixture of equal parts of a suspension comprising the spinal cord and culture, virus=containing fluid. Table 7 is representative of the results obtained after the virus isolation from the spinal cord at 36° and 40°C.

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Table 7

Isolation of attenuated poliovirus strains from the spinal cord during passages in monkeys.

Virus strain	Passage: Virus isolation from the spinal cord (lg.TCPD50 per 1 g of cord). at 36°C.									
	1	2	3	4	5	6	7	8	9	10
LSc,2 ab	3.3	3.9	3.7	4.2	4.0	3.6	3.5	4.4	3.5	3.6
P-712,Ch, 2 ab	3.6	3.7	3.5	3.8	4.3	3.9	4.2	3.5	4.4	3.6
Lecn,12 a_1b	2.1	4.9	5.3	4.3	4.6	4.8	4.4	6.0	4.9	5.2

continued

Virus strain	Passage: Virus isolation from the spinal cord (lg.TCPD50 per 1 g of cord). at 40°C									
	1	2	3	4	5	6	7	8	9	10
LSc,2 ab	0	0	0	0	0	0	0	0	0	0
P-712,Ch 2 ab	0	0	0	0	0	0	0	0	0	0
Leon,12,a_1b	0	0	1.8	3.2	4.6	3.3	4.1	5.6	4.2	5.0

Hence it is possible to isolate the virus from the cord of monkeys inoculated with attenuated poliomyelitis virus and sacrificed on the 6th day. We failed to note any perceptable changes in the virus titre in the course of passages. The types I and II virus strains could be isolated only at 36°C, while the type III

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at 40°C appeared already after the 3d passage, inclusive.

Genetic signs were investigated in the virus strains isolated from the spinal cord after the 3d, 6th and 10th passages. The resultant data are presented in table 8.

T a b l e 8.

Genetic signs of attenuated poliovirus strains following 3, 6 and 10 passages through the spinal cord of monkeys.

Virus strain	No. of pass.	Clin. manif. of polio. with i.c. inoc. of monkeys (N sign)	Morph. changes in the CNS (M sign)		Multipl. at differ. t° (T sign) TCPD50/ml)		Multipl. with diff. pH (d sign): PFU/ml)		plaque size in mm (S sign)
			atten. virus type	vurul. virus type	36°	40°	0.1% soda	0.4% soda	
Type I, LSc, 2 ab	3	0/4	1/4	0/4	7.1	1.0	4.8	7.2	-
	6	0/4	0/4	-	6.3	1.0	4.2	6.1	-
	10	0/4	0/4	-	7.4	1.0	4.9	7.1	4.6±1.3
Type II, P-712, Ch., 2 ab	3	0/4	0/4	-	6.0	1.0	3.9	5.8	-
	6	0/4	0/4	-	6.1	1.0	3.4	5.6	-
	10	0/4	0/4	1/4	5.7	1.0	3.6	5.7	4.4±1.1
Type III, Leon, 12 $a_1{}^b$	3	0/4	2/4	0/4	6.8	3.5	5.9	6.4	-
	6	10^0 4/4	10^{-1} 0/4	0/4	7.6	7.1	6.9	7.1	-
	10	4/4	1/4	0/4	7.3	7.0	7.0	7.1	7.5±4.2

The figures in table 8 show that the types I and II virus strains have retained their genetic signs similar to the initial strains throught all the 10 passages via the spinal cord of monkeysThe type III virus showed a certain chage in the T and d signs already after the 3d passage, while following the 6th passage by all its genetic signs it differed in no way from the virulent virus.

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Thus in this experimental series, just like in the preceding one, genetic changes experienced only the virus of the type III.

In the following set of investigations we proceeded with the study of genetic signs changes in attenuated poliovirus strains multiplying in the intestines of the vaccinated children. Children whose blood prior to immunization had no antibodies to any of the three poliovirus types and who were not carriers of any intestinal viruses were vaccinated per os with attenuated poliovirus strains. Three groups of children from various Children Homes were given a dose of 100 000 of TPCD50 per each child of of one of the three types of attenuated virus. On the 7th,14th and 28th days following administration of the virus it was isolated from the feces of the vaccinated children. A comparative study of the N and T signs was made in all of the isolated strains. Monkeys were inoculated intracerebrally with 0.5 ml of the culture , virus=containing fluid, which at the same time was titrated at 36° and 40°C. The results of this comparative study of the N and T signs in 85 strains of the poliomyelitis virus isolated from vaccinated children are incorporated in tables 9,10 and 11.

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T a b l e 1.

Comparative study of the "N" and "T" signs peculiar to [illegible]e strains of poliovirus, isolated from the feces of children vaccinated with the poliovirus [illegible] by Sabin.

No, No	The day of the strain isolation	[illegible] by [illegible] strain LSC, 2 ab. (In monkeys) Clinical manifestations of poliomyelitis in intra-cerebral infec.(N sign)		Virus multiplication at differ at temperatures [illegible]50/ml lg)	
		Undiluted virus	diluted 1:10	36°C	40°C
3.	[illegible]	0/3	-	6,2	1,0
2	28	0/3	-	5,4	1,0
4	28	0/4	-	5,9	1,0
5	I4	0/4	-	5,4	1,0
7	[illegible]	0/4	-	5,8	1,0
7	28	0/4	-	5,6	1,0
I0	I4	0/4	-	5,[illegible]	1,0
I2	I4	0/4	-	5,5	1,0
I4	[illegible]	0/4	-	6,0	1,0
I4	I4	0/4	-	5,6	1,0
I6	[illegible]	0 /4	-	3,8	1,0
I6	I4	0/4	-	5,9	1,0
I6	28	0/5	-	6,2	1,0
I7	I4	0/4	-	5,[illegible]	1,0
20	28	0/3	-	6,3	1,0
2I	I4	0/4	-	5,2	1,0
2I	28	0/3	-	6,I	1,0
22	[illegible]	0/4	-	5,[illegible]	1,0
22	28	0/4	-	5,5	1,0
23	[illegible]	0/4	-	6,6	1,0
25	I4	0/4	-	[illegible],3	1,0
26	I4	0/4	-	6,8	1,0
28	[illegible]	0/3	-	[illegible],[illegible]	1,0
28	I4	0/3	-	6,5	1,0
28	28	0/3	-	5,8	1,0
29	I4	0/4	-	6,I	1,0
30	I4	0/4	-	5,3	1,0
3I	I4	0/4	-	5,0	1,0
3I	28	0/4	-	6,2	1,0
32	I4	0/4	-	6,8	1,0
33	I4	0/4	-	5,I	1,0
34	I4	0/4	-	5,3	1,0
35	I4	I/4	0/4	[illegible],2	4,3
36	I4	0/4	-	[illegible],0	1,3
37	I4	0/4	-	6,[illegible]	1,0
37	28	0/4	-	6,2	1,0
38	I4	0/4	-	5,9	1,0
39	I4	0/4	-	6,0	1,0
40	I4	0/4	-	5,[illegible]	1,0
40	28	0/3	-	6,I	1,0

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Table 10.

Comparative study of the "N" and "T" signs peculiar to the strains of poliovirus, isolated from the feces of children vaccinated with the poliovirus attenuated by Sabin, type II, strains P-712, Ch, 2ab.

No, No	The day of the strain isolation	Clinical manifestations of poliomyelitis in intracerebral infec. of monkeys (N-sign)		Virus multiplication at different temperatures (T sign)-/TCPD50/ml /	
		Undiluted vir.	Diluted 1:10	36°C	40°C
65	I4	0/3	-	6,3	<I,0
68	I4	3/3	0/3	5,8	5,7
7I	I4	0/3	-	6,2	<I,0
72	[illegible]	0/4	-	6,[illegible]	3,I
72	I4	I/4	I/4	5,4	5,0
73	I4	0/4	-	6,0	<I,0
74	I4	I/4	0/4	5,6	3,0
75	I4	0/3	-	6,I	<I,0
76	I4	0/3	-	6,8	<I,0
77	I4	0/4	-	6,0	<I,0
78	I4	0/4	-	6,8	<I,0
78	28	0/3	-	6,I	<I,0
79	I4	0/4	-	5,6	<I,0
79	28	0/3	-	6,2	<I,0
8I	I4	0/4	-	6,2	<I,0
8I	28	0/3	-	6,7	I,0
82	I4	0/4	-	6,3	I,0
83	I4	0/4	-	6,7	2,6
84	I4	0/3	-	6,3	<I,0
85	I4	0/4	-	5,4	<I,0
86	I4	I/4	0/4	5,8	3,7
88	I4	0/4	-	6,9	<I,0
97	I4	0/4	-	5,7	<I,0
98	I4	0/3	-	6,2	<I,0
99	I4	0/4	-	6,8	<I,0
99	33	0/4	-	5,9	<I,0
I00	I4	0/3	-	[illegible]	2,7
I00	28	0/3	-	7,2	4,4

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T a b l e 11.

Comparative study of the "N" and"T" signs of the poliovirus strains isolated from the feces of children vaccinated with poliovirus attenuated by Sabin, type III, Leon 12 a,b.

No.No.	The day of strain isolation	Clinic. manifestations of polio. in intracer. inoc.of monkeys(N sign)		Virus propagation at differ.temper. (T sign)TPCD50/ml	
		indiluted	diluted 1:10	36°	40°
43	7	0/4	-	6,9	I,0
43	I4	3/3	0/3	6,6	3,7
43	28	I/4	0/4	5,0	4,7
44	I4	4/4	0/3	6,4	6,0
44	28	0/4	0/4	4,9	4,7
45	I4	I/4	I/4	6,4	4,8
46	7	I/4	0/4	6,7	6,0
46	I4	2/3	I/3	6,4	5,2
47	I4	0/4	-	6,4	<I,0
5I	7	2/3	0/4	6,3	4,2
52	I4	0/4	-	5,9	I,0
59	I4	0/4	-	6,8	I,0
60	I4	0,4	-	6,2	I,0
6I	7	0/3	-	7,I	I,0
6I	I4	I/4	0/4	6,5	5,6
62	I4	0/4	-	6,0	I,0
63	I4	0/4	-	7,3	3,2

From the data listed in tables 9,10 and 11 it follows that among the total of 40 poliovirus strains isolated from the feces of children vaccinated with the type I attenuated poliovirus strain it was only one strain (No.35) that produced clinical symptoms of poliomyelitis in intracerebral infection of monkeys. This strain was able to reproduce itself at 40°C. The rest of the strains failed to show any clinical manifestations of poliomyelitis and were not able to multiply at 40°C.

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Out of 28 poliovirus strains isolated from the feces of 22 children vaccinated with the type II attenuated poliovirus strain - 4 strains taken from 4 vaccinated children provoked clinical manifestations of poliomyelitis in intracerebral inoculation of monkeys and were able to propagate at 40°C. Of the remaining strains, which failed to produce any clinical symptoms of poliomyelitis ,all but four failed to propagate at 40°C. Of these four strains one (No.72/7 was isolated on the 7th day, while the virus isolated from the feces of the same child on the 14th day proved neuropathogenic for monkeys. (72/14). Two other strains were isolated from one vaccinated subject on the 28th day and 14th day (No.100), whereby the one isolated on the 28th day was seen to actively multiply at 40°C, although it failed to produce the actual disease in intracerebral infection of monkeys.

Out of 17 poliovirus strains isolated from the feces of 12 children immunized with the type III attenuated poliovirus strain- 8, taken from 6 vaccinated subjects produced a clinically pronounced form of poliomyelitis in intracerebral infection of monkeys and were capable of propagating at 40°C. Of the remaining 9 strains, which failed to produce clinical symptoms of the disease.- 2 propagated at 40°C. One of these was isolated from the feces of a child on the 28th day following vaccination, whilst the strain isolated in the same child on the 14th day proved neuropathogenic for monkeys.

It should be emphasized that in all instances showing deviations of the N and T signs- experiments were staged anew; whereby these control experiments invariably confirmed the primary results.

A supplementary study was made of 20 poliovirus strains in order to find out the correlation between the N and T signs. These strains were taken from clinically healthy children before vaccination. The results of the study are listed in table 12.

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T a b l e 12.

Comparative study of the "N" and "T" signs of the poliovirus strains isolated from the feces of clinically healthy children.

No.No. of strains	Virus type	(N sign) Clin.manifest. of polio. in intracerebr.inoculation of monkeys.			Virus multiplic. at different temper.(T sign- lg.TPCD50/ml)	
		Undiluted v.	dil. 1:10	dil. 1:100	36°	40°
I	I	I.3	I/4	0/4	5.9	2.6
2	I	3/4	I/4	I/4	6.4	4,2
3	I	2/3	I/4	0/4	5.7	4.0
4	I	0/4	0/4	0/4	6.7	3.0
5	I	3/4	I/4	I/3	6.6	4,3
6	I	2/4	2/4	0/4	7.I	4.4
7	I	2/4	I/3	I/3	5.9	4.2
8	I	2/3	2/4	0/3	7.0	5.2
9	I	2/4	I/3	0/4	6.6	3,3
IO	I	3/4	I/3	0/3	6.2	3.7
II	I	I/3	2/4	I/4	7.2	4.0
I2	I	2/3	0/4	0/4	6 0	5.2
16	I	I/3	2/4	2/4	6.4	4.5
2I	I	0/4	0/4	0/4	4.7	I.0
23	I	I/4	I/3	0/3	6.3	3,4
25	I	2/4	I/4	0/4	6.4	4.4
26	I	0/4	0/4	-	7,0	3,5
27	I	2/4	0/4	-	6,2	4,0
28	I	I/4	0/4	-	7,I	3,3
5I	III	0/3	0/3	-	4,3	I,0

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The figures included in table 12 indicate that 16 out of 20 strains investigated turned out to be neuropathogenic for monkeys in their intracerebral infection and were able to propagate at 40°C. Of the remaining 4 strains, which failed to produce clinical symptoms of poliomyelitis in intracerebral inoculation of monkeys, - two were capable of multiplying at 40°C.

Thus, comparative study of the N and T signs in 105 poliovirus strains showed coincidence of the N and T signs in the vast majority of them. All the 29 strains which provoked clinical manifestations of poliomyelitis in intracerebral infection of monkeys were able to reproduce themselves at 40°C. Among 76 strains, which proved non-pathogenic for monkeys following their intracerebral inoculation, it were only 8 that could multiply at the temperature of 40°C.

In 13 poliovirus strains, isolated from the feces of vaccinated children and which proved to be neuropathogenic for monkeys and multiplied at 40°C, - d and S signs were subjected to study. The results of these experiments are represented in table 13.

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T a b l e 13

The study of the "d" and "S" signs of the poliovirus strains isolated from the feces of vaccinated children.

No. No. of strains	Virus type	Multipl. with differ. pH (d sign) PFU-1g)		Plaque size in mm (S sign)
		0.1% soda	0.4% soda	
35/I4	I	7,0	7.I	7.I 3.5
68/I4	II	5 3	5 5	7 6 3 3
72/I4	II	5 2	5.2	7.I 3.7
74/I4	II	5,4	5 5	6.9 3 5
86/I4	II	5.I	5 0	7 2 3.7
43/I4	III	6,7	6.7	7.6 4.0
43/28	III	5.0	5.I	7 4.2
44/I4	III	6,8	6.5	7.9 4 2
45/I4	III	6 6	6,7	7.0 3.9
46/7	III	6,2	6.I	7.6 3 8
46/I4	III	7 0	6 8	7 7 4.3
5I/7	III	6.7	6.7	7.8 4.I
6I/I4	III	I	.2	7 6 3 9

As seen from the data in table 13 all the 13 strains which changed their N and T signs while multiplying in the intestine of the vaccinated children differed by the d and S signs from the initial attenuated strains.

It should be pointed out that morphological changes produced by these strains in the central nervous system of monkeys (N sign) did not differ from lesions developing during infection of monkeys with virulent poliovirus strains.

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Thus, the 13 poliovirus strains isolated from the feces of children vaccinated with live poliovaccine prepared from the Sabin's strains changed their initial signs, characteristic of attenuated strains (N,K,T,d and S signs).

Having obtained the above results we ~~xe~~ decided to find out whether the viruses isolated from the feces do actually stem from the Sabin's strains used in vaccination, or they were native policvirus strains, penetrating the ~~th~~ organism of children at the time of immunization. To solve this question we used the procedure of kinetic neutralization, suggested by Mc Bride (1959), with the help of which it is possible to differentiate individual virus strains within one and the same type according to the time-space required to neutralize the virus with specific antiserum.

In our experiments we studied 13 poliovirus strains isolated from the feces of vaccinated children having genetic signs different from those in initial poliovirus strains attenuated by Sabin and also from other virulent strains, known to be of different origin (serving as controls). Neutralization was effected with antesera obtained by immunizing rabbits with the poliovirus strains attenuated by Sabin. The results of these experiments are incorporated in ~~the~~ Table 14.

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T A B L E 14.

Identification of poliovirus strains isolated from the feces of children vaccinated with attenuated by Sabin poliovirus strains by kinetic neutralization method.

Type of the strain	Designation of the strain	Antiserum	The value of "K" with respect to the time interval of 15 minutes.
I	LSc,2ab	anti-LSc, 2 ab	22
	Brunden		11
	35/14		24
II	P-712,Ch.,2ab	anti-P-712,Ch, 2 ab	32
	MEF I		7
	68/14		34
	72/14		31
	74/14		32
	86/14		31
III	Leon,12 a_1b	anti-Leon, 12 a_1b	36
	Sockett		9
	43/14		36
	43/28		37
	44/14		39
	45/14		35
	46/7		37
	46/14		37
	51/7		36
	51/14		34

The Data of table 14 demonstrate that all the investigated strains, isolated from the feces of vaccinated children are indeed variants of the initial poliovirus strains attenuated by Sabin used in effecting the vaccination.

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Thus the last set of experiments served as a proof that in the course of multiplication of poliovirus strains attenuated by Sabin in the intestine of vaccinated children out of 40 type I virus strains it was only 1 that changed all the genetic signs studied by us (N,M,T,d and S signs). Of 28 type II strains all the of the genetic signs under investigations turned out to be different in 4 , while in 4 others of the same type it was only the T sign that has changed. Of maximal occurrence were changes of genetic signs in strains of the III type. Thus, out of 17 isolated strains initial genetic signs remained in only 7 of them. Changes in all of the signs under study were noted in 8 strains, while in 2 more it was the T sign that underwent a change.

D I S C U S S I O N.

The study of small batches of poliomyelitis viruses prepared at the Moscow Institute of virus preparations from strains attenuated by Sabin demonstrated the genetic properties of these strains to be different from those of virulent viruses. Apart from from the genetic signs mentioned in literature sources , which characterize the strains attenuated by Sabin(N,T,d and S signs) it was also disclosed that morphological alterations, produced by these strains in the central nervous system of monkeys differ not only qunatitatively, but also qualitatively from the picture peculiar to morphological lesions of the nervous system, observed following inoculation of monkeys with a virulent virus. This distinction permits it to single out one more sign, characteristic of the poliovirus strain attenuated by Sabin,viz;-the peculiarities of the morphological picture (M sign). It should be noted in this conjunction that in the work of Marie with collaborators (1959)there is also a mention of such qualitative

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distinctions in morphological changes of the central nervous system taking place in monkeys infected with poliovirus strains attenuated by Sabin, but it contained no detailed analysis thereof.

Our laboratory study of genetic properties peculiar to poliovirus strains attenuated by Sabin, carried out by passaging them on a culture of monkey's renal tissue at 40^0C demonstrated the high stability of genetic signs in the I and II types strains, and a substantially lower one in the strain of the III type. We did not succeed in in obtaining any changes in the genetic properties of strains LSc,2 ab, typeI in passaging them at 40^0C. But, as pointed out by Lwoff (1959), and also by Sabin (1959b), a prolonged passage of this strain at 41^0C resulted in turning it into neuropathogenic one for monkeys during their intracerebral infection. It is to be noted that this variant, although it has changed the N sign, nevertheless retained a substantial feature peculiar to the initial strain,viz;-inability to produce a recognizable viremia (Sabin,1959b).

In the second series of experiments we studied changes in genetic signs in poliovirus strains attenuated by Sabin in the course of passages in the spinal cord of monkeys of the Macaca=rhesus genus. Normal temperature of the monkeys in general comprises 38-39^0C. By staging special experiments we gained certitude that the level of temperature in their cord fluctuates around 39^0C. In these passages, therefore, the thermal factor was quite essential. In these our experiments, like in the preceding ones, genetic signs of the type I and II strains proved extremely stable and were not liable to any change in the course of 10 passages. On the other hand, the strains of the III type, beginning from the 6 passage, changed all their

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genetic properties (N,M.T,d and S signs).

The last set of experiments was devoted to the study of genetic signs specific to poliovirus strains isolated from the feces of children vaccinated with live poliovaccine prepared from the Sabin's strains. In these experiments genetic properties proved most stable in the type I strain. Of 30 investigated strains of this type it was only one that showed any changes in its genetic signs. Of 28 strains of the II type genetic properties experienced complete change in 4,and partial- in 4 more strains. Of 17 strains of the III type - 8 changed all their genetic signs, while in 2 of them it was only T sign that became altered.

Hence,this part of our investigations showed that in the course of virus multiplication in the intestine of children, where the number of reproduction cycles is infinitely higher than under laboratory conditions, changed genetic signs could be seen not only in the type III strain, but in that of the type II and even in the strain of the I type, too.

In these experiments subject of study was comparative investigation of N and T signs in 105 strains of poliovirus. It was shown that all the 29 strains, which produced clinical symptoms of poliomyelitis in intracerebral infection of monkeys, were able to multiply at 40°C. Among 76 strains,non=pathogenic for monkeys during their intracerebral inoculation, there were only 8 that could propagate at 40°C. It should be noted that in experiments conducted by Paul with coll.(1959)and by Benyesh-Melnick and Melnick (1959), just like in ours, all of the poliovirus strains causing paralysis in intracerebral infection of monkeysmultiplied at 40°C.The N sign, apparantly, is more closely connected with with the T sign than with of d. As known, it is by far not always that the correlation between the d and

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N signs can be observed (Sabin,1959b, Benyesh-Melnick,Melnick, 1959).

The isolation of strains with elevated neurotropism from the feces of children vaccinated with poliovirus strains attenuated by Sabin is by no means a novely. This has been shown by many authors (Clarke with coll.,1958, Benyesh-Melnick and Melnick,1959, Sabin,1959a,b, Horstmann with coll.,1959,Melnick with coll.1959,Paule with coll.,1959, Stuart-Harris,1959)Sabin(1959b), however, holds that in studying neuropathogenicity for monkeys of strains isolated from the feces of vaccinated humans one should take acount of the fact that the virus, which multiplies in the intestinal tract of man at 37-38°C, when it reaches the nervous system of monkeys has a temperature of 38-40°C. There, according to him, neuropathogenic particles are subject to a further selection, as the result of which the virus may bring forth clinical manifestations of poliomyelitis. Because of this, according to Sabin, the evaluation of neuropathogenicity of poliovirus strains isolated from the feces of vaccinated humans on monkeys may not reflect the true nature of the virus isolated from the intestine.

We cannot agree with the said opinion expressed by Sabin, since, on the one hand, we have a conclusive proof to the effect that, along with with the elevated neuropathogenicity for monkeys, the virus strains,isolated from the feces of vaccinated children, there occur changes also in their other genetic signs, the evaluation of which does not involve any supplementary virus selection. On the other hand, our experiments for the study of changes occurring in genetic properties of poliovirus strains attenuated by Sabin during their passages in the spinal cord of monkeys demonstrated that during these passages,i.e. at the time

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of virus reproduction in the nervous system of monkeys, either there was no selection of neuropathogenic particles at all (for the type I and II strains), or else could be observed only after a considerable number of passages (following the 6th passage for the III type).

One of the essential features of poliovirus strains attenuated by Sabin is their inability to produce a recognizable viremia, as was shown for the types I and III; while the type II is capable to produce but a very weak and short-livd xeiremia (Sabin,1y5yb, Gear, 1y5y). This property of the strains is, probably, the most important one, since it precludes the virus penetrating the central nervous system. It is but natural that, while studying changed genetic properties of poliovirus strains attenuated by Sabin, this feature should be taken account of, too. As already indicated before, the strain LSc, 2 ab, which became neurotropic for monkeys after a number of passages at 41°C , (Lwoff,1y5y), as before, had an extremely low power to produce vireria and call forth paralyses in intravenous infection of young monkeys (Sabin,1y5yb). From practival viewpoint,therefore, the variants of poliovirus strains attenuated by Sabin , having elevated neurotropism for monkeys, but incapable of producing recognizable viremia, present actually no danger for the organism. On the contrary, when the strains, along with the changed N,T,d and other signs, become capable to produce viremia to a considerable degree,their menace for man becomes unquestionable.

In this connection we deem it extremely important to supplement the study of the changes in the N,M,T,d,S and other genetic propetries with that of the ability of strains to produce massive viremia, by paying to this last-named problem especial attention. This, in the first place, refers to the strains isolated from the feces of vaccinated children. Investigations to

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to this effect are being conducted by us at the present time.

C C N CL U S I O N S.

1. The study of a small batch of poliovirus, produced at the Moscow institute for virus preparation from the poliovirus strains attenuated by Sabin revealed them to essentially different from virulent strains by a series of genetic properties(N,T,d and S).

2. Introduced into the central nervous system of monkeys the poliovirus strains attenuated by Sabin give rise to the development of a peculiar morphological picture, which qualitatively differs from the usual one,observed during experimental poliomyelitis consequent upon infection with virulent strains. These distinction may be designated as the M sign of attenuation.

3. Following 10 passages of poliovirus strains attenuated by Sabin on a tissue culture of monkey kidneys at 38^0 and 40^0C, and also through the spinal cord of monkeys, genetic signs of the types I and II strains remained unchanged. The type III strain lost all of the investigated genetic properties specific to the initial attenuated virus (N,M,T,d and S).

4. The study of genetic signs particular to the polivirus strains isolated from the feces of children vaccinated with live poliovirus vaccine prepared from Sabin's strains, demonstrated the investigated signs to be most stable in strains of the type I, somewhat less so in those of the II type, and least stable in the strains of the III type.

5. Special experiments involving kinetic neutralization made it possible to demonstrate that the strains with changed genetic signs, isolated from the feces of vaccinated children, represented variants of polivirus strains attenuated by Sabin, which

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had been used for the immunization.

6. A comparative study of the N and T signs in 105 poliovirus strains has shown that of those, which were neurotropic for monkeys in their intracerebral infection, all were capable of multiplying at 40°C. Of 76 strains, which failed to produce clinical symptoms of poliomyelitis, following intracerebral inoculation of monkeys, there were only 8 that could propagate at 40°C.

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Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

BIBLIOGRAPHY.

1. Gendon,Yu.Z.,Levenbuk,I,S.,Genkina,F.B.,Maltseva,L.Z.
Vestnik AMN SSSR,1959 , in the process of publication.

2. Ginsburg,N.N, J.M.E.I.,1947,7,3.

3. Ginsburg,N.N., Problems of virology,1959,5; 620.

4. Robinson,I.A..In the book " Epidemic Poliomyelitis,Moscow, 1957, 58.

5. Smorodintsev,A.A.Ilyenko,V.J.,Kurnosova,M.M, Gorgev,N.J., Zhilova,G.P.: First Intern.Conf. on live Poliovir.Vacc.,1959, 22-26 June, Washington,312.

6. Chumakov,M.P, Voroshilova,M.K., Vasilieva,K.A.,Bakina,M.N., Dobrova,I.I., Drozdov,S.G., Podsedlovsky,T.S., Kostina,K.A., Shirman,G.A.,Yankevich,O.D., Uspensky,Yu.S., Ashmarina,E.A. Problems of virology, 1959,5,520.

7. Ramos-Alvarez,M.N.,Santos F.S., Rivery,LR.,Mayes,O.,First Intern.Conf. on Live Poliovir.Vacc.,1959,22-26 June, Washington,483.

8. Benyesh-Melnick M., Melnick J.,Idem,179

9. Bodian,D.Bull.John's Hopkins' Hosp.,1948,83,1,1.

10. Cabasso,V.,Jervis G.,Moyer,A.,Roca-Garcia,M,Orsi,E.,Cox,H. First Intern.Conf.on Live Poliovir.Vacc.Washington 1959,22-26 June,102.

11. Clarke,S.,Goffe,A., Stuart-Harris,C.,Herrog,E.,Brit.Med.J. 1958,5106,1188.

12. Dulbecco R,Vogt,M, Virology,1958,5,2220.

13. Gear,J.,First Intern.Conf. on Live Poliovir.Vacc.,Washington, 1959,22-26 June,154.

14. Hale,J.,Doraisinghan,M.,Lee,L.,Kanagaratnam,Leong,K,Monteiro, E., Idem,286.

15. Horstmann,D., Niederman,J.,Paul,J.J.A.M.A.,1959,170,1,1.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

16. Hsiung,G.,Melnick,J,J.Immunol.,1957,78,2,128.

17. Hsiung,G.,Melnick,J.,J.Immunol.,1958,80,4,282

18. Jezierski,A.,Ann.Soc.belge.med.trop.,1959,39,1,69.

19. Koprowski,H.,Idem,1958,38,2,327.

20. Lwoff,A.,Lwoff,M.,Compt.rend.Ac.Sci.,1958,246,1,190.

21. Lwoff,A.,Lwoff,M.,Idem,1959a,248,1,154.

22. Lwoff,A.,Lwoff,M.Idem,1959b,248,1725.

23.Lwoff,A.Bact.rev.,1959,7,1,45.

24. Mc Bride,W.,Virology,1959,7,1,45.

25. Murray,R.,Kirschstein,R.,Van Hoosier,G.,Baron,S.First Intern. Conf. on Live Poliovir.Vacc.,1959,22-26 June, Washington,39.

26. Melnick,J.,Benyesh-Melnick M.,Brennan,J.J.A.M.A.,1959,171,9 1165.

27. Paul,J.,Horstmann,D.,Riordan,J.,Wiederman,J.,Gochioke,J., First Intern.Conf.on Live Poliovir.Vacc.,1959,22-26 June, Washington,218.

28. Sabin,A.,Ann.New-York.Ac.Sci.,1955,61,984.

29. Sabin,A.,J.A.M.A.,1957,164,11,1216.

30. Sabin,A.,Brit.Med.J.,1959a,5123,663.

31. Sabin,A., First Intern.Conf.on Live Poliovir.Vacc.,1959b, 22-26 June,Washington,14.

32. Sabin,A., Idem,1959b,35.

33. Sabin,A.,Directions for preparation, testing and assay of oral,live poliovirus vaccine,1959,August 19.

34. Skovranek,V.,Zacek,K.,Verma,V.,Adam,B.,Adamova,V.,Bucian,V., Vogtova,H.,First Intern.Conf.on Live Poliovir.Vacc. 1959,22-26 June,Washington,530.

35. Stuart-Harris,C. Idem, 339.

36. Verlinde J.,Wilterdink,J.,Kret,A.,Arch.ges.Virusforsch., 1959b,5,549.

37. Vogt,M.,Dulbecco,R.,Wenner,H..Virology,1957,4,141.

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Fig. 1.
Perivascular infiltrate within the area of introduction of 0.5 ml of the virus attenuated by Sabin into the thalamus of a monkey. Stained with hematoxilin and eosin. Magn. 170x.

Fig.2.
Destruction of neurones and inflammatory infiltration in the anterior horn of the grey matter of the 3d lumbar segment in the vicintiy of the site, where 0.5 ml of indiluted virus, attenuated by Sabin,was introduced(Type I). Stained with tionine after Nissle Magn.?0x.

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Fig. 3.

Lesion of the Clarke's nucleus and perivascular infiltrates in the second lumbar segment of the spinal cord of the same monkey as shown on fig.2. Stained with tionine after Nissle, Mag.20x.

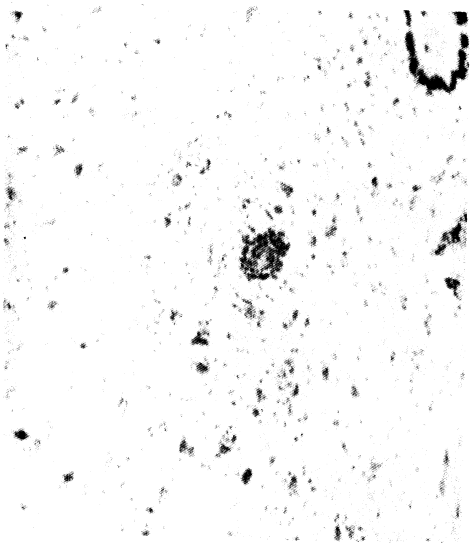

Fig. 4.

Perivascular infiltration and moderately pronounced changes of nervous cells in the gray matter of the 6th cervical segment of the spinal cord in a monkey which showed spreading of pathological changes beyond the limits of the lumbar region of the cord during intraspinal administration of 0.5 ml of indiluted virus. Stained with tionine after Nissle, Magn.60x.

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THE THERMAL MARKER METHOD IN CONTROL OF LIVE VACCINE

G.A.Shmeleva, S.G.Dsagurov

The Biological Control department at the Poliomyelitis Institute of the AMS USSR.

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THE THERMAL MARKER METHOD IN CONTROL OF LIVE VACCINE

G.A. Shmeleva, S.G. Dsagurov

(The Biological Control department at the Poliomyelitis Institute of the AMS USSR).

The genetic stability of the poliovirus attenuated strains is one of the most important issues arrising in the preperation and use of live poliovirus vaccine.

For the production of live vaccine at our Institute it is only the material of the first passage taken from the author's own bottles of attenuated Sabin strains that is being used as culture material. This serves as a guarantee against all kinds of accidental changes in the characteristics of the vaccine during its passages. Nevertherless, the control system adopted in our Institute in the production of live poliovirus vaccine provides for a certain measure of identification of attenuated vaccinal strains by the titration effected simulteneously at 36^0 and 40^0 C.

We did not consider this complementary identification of the live vaccine strains to be superfluous, although according to official instructions the thermal marker method is not held to be obligatory.

With this aim in view, while conducting daily routine tests of each new batch of live vaccine (until unifying the batches into series) we succeeded in accumulating some factual data which could form a basis for resolving the problem respective the expediency of using the thermal marker as a regular feature in the production of live vaccine.

The titre verification of the vaccinal virus was done by the method of rotating test-tubes containing seven-day monostratal cultures of trypsinized monkey renal cells.

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The live vaccine batches were titrated at +36° C and +40°C with two test=tubes used for an each dilution, the dilution series having an interval of I logarithm.

0,2 ml of the corresponding dilution and I,8 ml of the medium № I99 without vaccine were placed into each test=tube. The titration results were estimated on the 7-th day. The results of our work are given in the table appended hereto.

The table includes the numbers of titrated vaccine batches and the numbers of the series, which comprised the virus batches titrated at different temperatures.

The thermal marker was used by us in a total of II4 vaccinal virus batches comprising 24 series of live poliovirus vaccine. The examination results of all the batches differed but very little from each other, and therefore, in order to keep the table free from supperflous figures, we indicated therein only selective titration results. The verification of live poliovirus vaccine batches by the method of the thermal marker showed the termal sign in attenuated polioviruses to be constantly present throughout the entire cycle of the live vaccine production. This sign conformed to the characteristics of the weakened neurovirulence of the vaccinal strains. The average difference between the virus titres verified at the indicated above two temperature levels was as high as 500 000 – 1,000,000 times.

The polioviruses in the batches tested by us were the second passage material of A.B. Sabin's original strains.

It is believed that in the production of live poliovirus vaccine the thermal sign is of a stable nature, and it should be given due consideration while exercising control of the vaccine in the tissue culture.

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Table

RESULTS OF THE VERIFICATION OF LIVE POLIOVIRUS VACCINE LOTS BY THE METHOD OF THERMAL MARKER

Type	No. of lots and series		TCD50 Titre at +36°C	TCD50 Titre at +40°C
I	89	35	7.2	I.0
	90	35	7.2	I.0
	94	35	7.2	I.0
	77	35	7.2	I.0
	87	35	6.7	I.0
	93	35	7.2	I.0
	85	35	6.7	I.0
	9I	35	6.2	I.0
	92	35	6.2	I.0
I	I09	38	7.7	I.0
	III	38	6.7	I.0
	II4	38	7.2	I.0
	II6	38	7.2	I.0
	II7	38	7.2	I.0
	I04	38	6.2	I.0
	I05	38	6.7	I.0
	I06	38	7.7	I.0
I	I32	4I	6.7	I.0
	I22	4I	6.7	I.0
	I36	4I	6.7	I.0
	I3I	4I	7.2	I.0
	I33	4I	6.7	I.0
	I34	4I	6.7	I.0
	I38	4I	7.2	I.0
	II8a	4I	7.2	I.0
I	I59	44	6.7	I.0
	I60	44	7.2	I.0
	I62	44	6.7	I.0
	I63	44	7.2	I.7
	I64	44	6.7	I.0
	I65	44	7.2	I.0
I	I67	45	7.2	I.0
	I68	45	6.7	I.0
I	I75	46	7.2	I.0
	I76	46	7.2	I.0
	I77	46	7.2	I.0
I	I86	56	7.2	I.0
	I88	56	7.2	I.0
II	56	3I	7.2	I.7
	57	3I	6.2	I.0
	59	3I	5.7	I.0
II	60	33	7.7	I.7
	6I	33	6.7	I.0
	64	33	7.2	I.0
	70	33	6.7	I.0

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continued

Type	No. No. of lots and series		TCB50	
			Titre at 36°C	Titre at 40°C
II	101	36	6.7	I.7
	107	36	6.2	I.0
	110	36	7.2	I.0
	97	36	6.2	I.0
II	103	40	7.2	I.0
	108	40	6.7	I.0
	119	40	6.2	I.0
	120	40	6.7	I.0
	129	40	6.7	I.0
I	183	52	6.7	I.0
	184	52	7.2	I.0
III	41	27	7.7	I.7
	42	27	7.7	I.7
	44	27	7.7	I.7
III	43	28	7.7	I.7
	45	28	7.2	I.7
	34	28	7.2	I.7
III	170	49	6.7	I.0
	171	49	7.2	I.0
	169	49	7.2	I.0
	166	49	7.2	I.0
III	172	50	6.7	I.0
	173	50	6.7	I.0
	178	50	7.2	I.0

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On the Difficulties due to Spontaneous Infections Arising During the Morphological Safety-tests for Polievaccines in Experiments on Monkeys

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A. M. S. U S S R

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With respect to the increasing use of monkeys for the practical and theoretical virology, there appeared an imperative need for extensive investigations of spontaneous infections in these animals.

Morphological studies of spontaneous neuroinfections were found to be of a paramount importance, since unsufficient knowledge of such maladies quite frequently leads to a serious difficulty in stating the differential diagnosis. However, the pathologist is obliged to conduct morphological safety tests of live and killed poliovaccines.

Investigations so far effected in this field are few and based chiefly on the study of individual cases which, however, aethiologically remain obscure (I, 2, 3, 4, 5).

It is recently, that as a result of large-scale examination of the nervous system in monkeys used for morphological tests on poliovaccines, there appeared individual works whose authors make an effort to systemize all morphological findings according to different viral agents (6, 7).

Among the diverse inflammatory changes in the central nervous system which were found in the course of morphological safety-tests on live and killed poliovaccines, our attention was fixed on isolated lesions of the medulla oblongata, observed in IO cases, this comprizing I,3 % of all the examinations made during I958-59.

In all cases in the group under consideration the administration of dead or live poliovaccine, the clinical observations, the sacrificing of the animals, autopsy and the withdrawal of material for histological studies were performed in conformity with the existing instructions on the testing of vaccines. In the majority of the cases the serial sections were prepared from the medulla oblongata and stained with hematoxylin and eosin and after Nissl. In addition to these the sections from medulla oblongata were stained with picrofuchsin and after Miyahava for microglia.

Microscopic investigations of the central nervous system had revealed that the inflammatory lesions, as a rule, were localized in the solitary nucleus and its tract (nucleus

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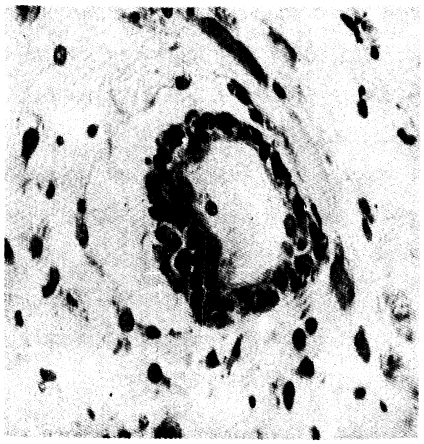

Fig I. Perivascular infiltration, composed , predominently of poliblasts and lymphoid cells. Nissl's staining method; magnification - x I0.

Fig 2. An infiltration composed of loosely distributed lymphoid cells ~~inthe~~- in the glossopharyngeal root matter. Hematoxylin and eosin; magnification - I0 x I0.

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tractus solitarii et tractus solitarius) as well as in descending nucleus of the trigeminal nerve (nucleus tractus nervi trigemini et tractus spinalis nervi trigemini). Less often, although quite constantly, the inflammatory changes were found in fila radicularia region of the glosso-pharyngeal nerve and in leptomeninges of the medulla oblongata, pre-eminently in region of the root departure of the trigeminal nerve. Sometimes these changes were found in the dorsal nucleus of the vagal nerve, in the subependimal zone of the IV ventricle, in reticular formation, in the matter of Hover's fascicule and in some other portions of the medulla oblongata.

The pathohistological pattern of the inflammatory lesions observed in medulla oblongata comprised perivascular infiltrations in the brain matter and meninges, nodular glial proliferations and the zones of glial hyperplasia.

The above components of the pathological picture did not occur with uniform constancy. Although the glial proliferations were manifest in all the cases without exception, and the perivascular infiltrations in the majority of our findings (7 cases), the diffuse glial hyperplasia was observed relatively less frequently (4 cases).

Perivascular infiltrations of the brain matter and the glial proliferations were limited in respect to their number and extent. Thus, the number of both of these types of lesions inthe medulla oblongata matter varied in different cases from 2-3 to 8-I0. Dimentially their ~~dia-~~ average diameter varied from 80 to I00 microns and never exceeded I50.

The focal perivascular infiltrations in the brain matter were localized around the capillaries or very small veins and were usually arranged in compact layers composed of one or two, rarely three, lines of cells (Fig. I). Considerably less often the perivascular accumulations were composed of irregularly and loosely distributed cells. The elements which build up these infiltrates represented plasmocytes, histoid and lymphoid cells and polyblasts as well. Quite often in the vessels surrounded by the above described cell accumulations it was possible to note the activation of endothelial cells,which was manifested by swelling of the latter. In some instances the proliferation of adventitial elements was quite prominent and we were

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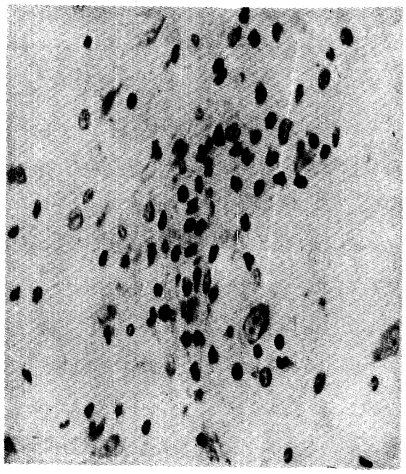

Fig 3; Glial nodule composed of loosely distributed microgliocytes, mixed with singular elements of oligidendroglia. Nissl's staining method; magnification - IO x IO.

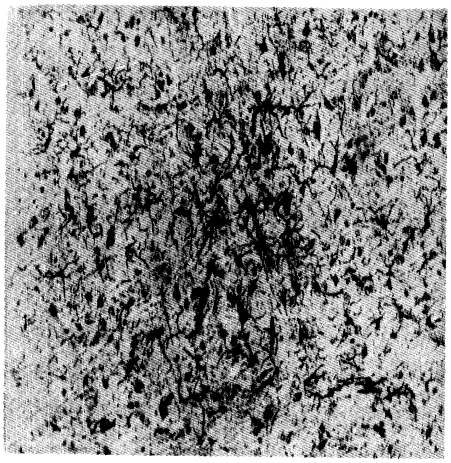

Fig 4. Hypertophied cells of microgliabuilding a nodule. Miyahava's staining method ; magnification - 7 x IO.

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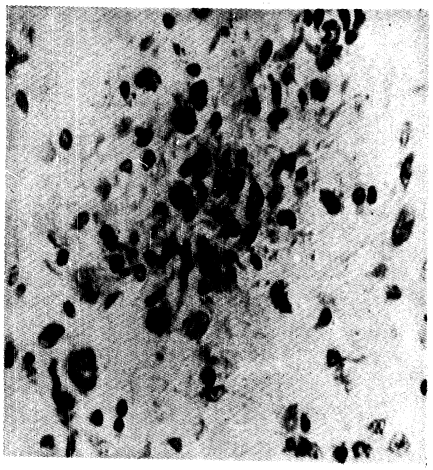

Fig 5; Microglial nodule composed of cells distributed in a form of a rosette. In the centre of a nodule you may see a structureless granular necrotic mass. Nissl's staining method; magnification - X IO.

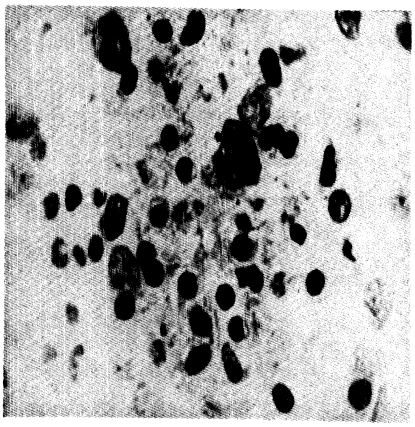

Fig 6. Among the cells of microglia ,building a nodule you may detect well seen unimpaired nerve cells. Nissl's stain; magnification - x IO.

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In addition to these "pure" perivascular infiltrations and "pure" glial nodules we revealed sometimes the mixed forms which were composed of vascular elements as well as of microgliocytes.

As mentioned previously, the third component of the histological pattern characteristic of the lesions observed, comprised the evidence of diffuse glial hyperplasia. It should be noted, however, that the latter may be named "diffuse" only conditionally, because it was , as a rule, limited by certain areas: particularly by the zone of solitary nucleus and its tract, by the descending nucleus of trigeminal nerve and its tract and by the region of fila radicularia. The hyperplasia serving as a background, against which all the above described focal changes were detected, was mildly manifested and was of a purily microglial nature.

Completing our description of the histological changes it must be mentioned, that we never observed any evidence of neuronophagy or of the neurons' desintegration. This was true for the foci themselves and for the neighbouring areas as well. Sometimes it seemed surprising that the nerve cells remained safe, being distributed among the elements of the glial nodules; (Fig. 6). The stereotype degenerative changes in nerve cells (tigrolisis and vacuolization), which appear in some instances, from our point of view, cannot be referred to the described lesions as they were present in other portions of the central nervous system. A picture of a perineural oligodendroglial satellitosis, which was found in some cases, was also not associated with the pathology of these derangements.

To summarize, it should be said that during the microscopic studies of the remaining portions of the central nervous system we were not able to disclose any pathological changes, except for the foci of the injuries due to the introduction of poliovaccine and the tissue reaction there to.

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The results of our microscopic investigations show that in all instances we were able to reveal more or less similar morphological changes, which give us the right to speak of a certain morphological syndrome. The similarity of morphological

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changes was determined on the basis of the following features:

I), the persistance of inflammatory changes localization in the medulla oblongata sensory formations;

2), the limitation of the inflammatory process and

3), the pre-eminently productive form of the inflammatory changes with a simultaneous survival of the neurocellular elements.

A markedly pronounced predominance of a productive component in the histological picture makes it possible to refer thes changes to the subacute forms of the inflammation, although sometimes they could be considered as residual changes. The latter may apparantly include also the cases which were histologically characterized exclusively by focal and diffuse glial proliferation in the abscence of vascular reactions and by the perivascular infiltrations in particular.

What could be the nature of an agent eliciting the described syndrome?

Confrontation of our data with those described in literature makes it possible to consider virus B (a virus attributed to the Herpes group and widely distributed among monkeys) as an agent aethiologically responsible for the lesions developing in the medulla oblongata (7, 8, 9, IO, II). A surprising similarity of the observed morphological pattern with findings described by Bodian (6) and Keeble (7) may serve as a confirmation to our assumption. Aethiologically those were proved to be associated with virus B basing on the serological and virological methods. This similarity was related to the localization of lesions and to the main histological features as well. It could be easily established despite the incompleteness of histological descriptions made in these communications.

Should such be correct, than , proceeding from the features peculiar to the localization of the process, from the nature of histological findings and some literature data, it is possible to give certain consideration on the pathogenesis of the infection produced by the virus B.

As it was previously indicated the process was maximally localized in the solitary nucleus and in descending nucleus of trigeminal nerve with their tracts, in fila radicularia and in the roots of glossopharyngeal nerve. It is well known that these

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anatomical structures are joined with each other by sensory gustatory fibers ending in solitary nucleus which plays a role of a collector accumulating all the sensations of taste and serving as a primary centre of gustation, (I2)(I3). At the same time, according to the studies of Keeble and his associates, it is quite evident that during the natural-~~affection~~ infection of monkeys with virus B the most prominent changes develope in a lingual region. Moreover, the changes in the medulla oblongata similar to the above described syndrome could be reproduced only as a result of introduction of virus into the subepithelial layer of the tongue (7), while the other experimental ways of infection (intradermal, intraperitoneal,intracerebral) were not able to reproduce such changes in the central nervous system. However, if in our cases there was an appearance of lesions in the central nervous system, they were always quite unsimilar to those described above (7, I4).

Thus, there apears an impression that during the natural infection of monkeys with virus B, the latter penetrates into theepithelium of the tongue and than passes within the gustatory ~~se~~ sensory fibers into the formations of the medulla oblongata and thus determining the display of pathological processes in these structures.

Being penetrated into the central nervous system, the virus however, shows no signs of the pronounced neurotropism, an evidence of which could be the survival of the nerve cells in the affected areas. The arising vascular and microglial reactions, which may be evaluated as the primary responses (because the nerve cells were not affected by virus) indicates to a rather mesotropic effect of virus B. In some respect this confirms the data of Sabin and Hurst (I4).It is possible that virus B possesses certain gliotropic properties as well. The ~~latter~~ last statement could be substantiated by the morphological findings of micronecrotic areas in the glioreticular substance of the brain.

An ~~aq~~ acquaintance with the described syndrome of the central nervous system impairment in monkeys has a certain practical significance for the pathologist, who conducts the morphological safety-tests on live or killed polievaccine. It is

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important because the localization of the pathological changes in the medulla oblongata, the forms of the inflammatory lesions and some oter peculiarities of this syndrome may cause a difficulty in differentiation of the latter with aparalytic forms of poliomyelitis. In overcomming the appearing difficulties in the differential diagnosis the whole morphological complex has to be brought under consideration. The features comprising this syndrome morphological complex, from our point of view, should include: extreme limitation of the pathological process, its localization in certain sensory nuclei of the medulla oblongata (solitary nucleus and descending nucleus of the trigeminal nerve) with derangement of glossopharyngeal nerve roots, apparant predominance of productive changes in the histological pattern of lesions and, at last, the unimpairment of neuro-cellular elements.

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Experimental study of the sensitivity to chlorine of attenuated and virulent strains of poliomyelitis virus and their adsorption by various kinds of soil

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The live poliomyelitis vaccine induces a benign infection with intensive multiplication of the vaccine virus in the intestinal tract of the vaccinated. Besides, it differs from other vaccines by its ability of spreading from the vaccinated to the unvaccinated individuals. During mass vaccination with the live polio vaccine a great quantity of vaccine virus is excreted with the faeces of the vaccinated into the outside environment.

In connection with this fact the study of the process of spread of the vaccine virus among the population should include an investigation of its behaviour in the outside environment.

The aim of the present work was a comparative study of the sensitivity to chlorine of attenuated and virulent strains of poliomyelitis virus and several enteric viruses and their adsorption by various kinds of soil.

For the experimental study of the effect of chlorine, suspensions of viruses containing $1.6 \times 10^3 - 16.0 \times 10^3$ $TCID_{50}$ per ml. were prepared on chlorine demand-free buffered distilled water at pH 6.3 - 6.8. The chlorination was carried out at a temperature of 18 - 23 ^{0}C; the initial doses of chlorine were such that after 30 minutes of exposure of virus to chlorine the concentrations of the residual chlorine in different experiments were from 0.1 to 1.5 mg/L with an interval of 0.1 mg/L. Every virus strain was tested in 30 to 80 experiments. Every sample of chlorinated water after required period of exposure was dechlorinated and its infectivity was tested by inoculating 0.2 ml. of water into each of four tubes with monolayer monkey kidney cell cultures. All the tubes were observed for 10 days

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after inoculation; on the basis of the results obtained the concentration of residual chlorine, in mg/L, giving 50% inactivation of virus (ED_{50}) was calculated by the Reed-Muench formula.

The results obtained indicated that A.B. Sabin's attenuated strains of all three types of poliomyelitis virus are more resistant to chlorine than all the virulent strains of poliomyelitis virus including Mahoney of I type, MEF-I of II type, Saukett of III type and Coxsackie B_3, ECHO-7a and ECHO-9a viruses too (Table 1).

The most resistant to chlorine of the vaccine strains was P-712.2ab of II type (ED_{50} - 0.92 mg/L), then LSc,2ab of I type (ED_{50} - 0.80 mg/L) and the least resistant was Leon 12, a_1b of III type (ED_{50} - 078 mg/L).

Among the investigated virulent strains of poliomyelitis virus a considerably higher resistance was displayed by Mahoney strain of I type (ED_{50} - 0.66 mg/L). The rest of the strains of II and III type of poliomyelitis and those of Coxsackie and ECHO viruses display a much lesser and almost equal degree of resistance to chlorine (ED_{50} - 0.37 - 0.41 mg/L). Consequently, no specific resistance to chlorine could be detected in definite kinds of enteric viruses or definite types of poliomyelitis virus.

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Table 1

Resistance to chlorine of attenuated and virulent strains of poliomyelitis and other enteric viruses in water (30 minutes exposure to chlorine)

No.	Virus strain	Serologic type	Virulence	ED_{50} Residual Cl. mg/L	
1.	Polio P-712,Ch,2ab	11	attenuated	0.92	0.03
2.	Polio LSc, 2ab	I	attenuated	0.80	0.02
3.	Polio Leon 12 alb	III	attenuated	0.78	0.04
4.	Polio Mahoney	I	virulent	0.66	0.03
5.	ECHO	7a	-	0.41	0.04
6.	Coxsackie	B_3	-	0.40	0.03
7.	Polio Saukett	III	virulent	0.38	0.04
8.	ECHO	9a	-	0.38	0.04
9.	Polio MEF-1	II	virulent	0.37	0.04

A detailed statistical analysis of the results obtained has demonstrated a sufficient reliability of the differences in the degree of resistance between the attenuated and the virulent strains of poliomyelitis virus of corresponding types and that between the least resistant of the vaccine strains (III type) and the most resistant of the virulent strains of poliomyelitis and that of Coxsackie and ECHO viruses (Table 2).

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Table 2

The reliability of the differences in the degree of resistance of attenuated and virulent strains of poliomyelitis and other enteric viruses

Attenuated strains polio virus		Virulent strains of polio a. enteric viruses		Difference ED_{50} Cl mg/L		Reliability test t
Type strain	ED_{50} Cl mg/L	Virus type	ED_{50} Cl mg/L			
I L Sc,2ab	0.80	Polio I	0.66	0.14	0.04	3.5
II P-712,Ch, 2ab	0.92	Polio II MEF-I	0.37	0.55	0.05	11.0
III Leon 12, a_1b	0.78	Polio III Saukett	0.39	0.39	0.05	7.8
-"-	0.78	Polio I Mahoney	0.66	0.12	0.05	2.4
-"-	0.78	Coxsackie B_3	0.40	0.38	0.05	7.6
-"-	0.78	ECHO-7a	0.41	0.37	0.05	7.4

The dynamics of the inactivation of various strains of poliomyelitis virus has been studied in connection with the chlorination of water. Comparative tests were carried out with different strains of viruses with similar doses of chlorine. In various tests the concentration of residual chlorine was from 0.35 to 0.9 mg/L. After different intervals of exposure from 2 1/2 to 90 minutes long, the water samples were dechlorinated and the amount of active virus present was determined by titration on monkey kidney cell cultures.

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Table 3 presents the data of one of 4 series of tests which gave similar results. The data obtained indicate that longer periods of exposure were required for inactivation of the attenuated strains of poliomyelitis virus than those required for the virulent strains.

In some cases the virus was not inactivated even after the maximum exposure to chlorine in spite of the fact that the concentration of the latter was high. However, the main fall in the virus titer always occurred after the first 2 1/2 minutes of exposure (Table 3).

Table 3

Dynamics of inactivation of the attenuated and virulent strains of poliomyelitis virus ($TCID_{50}$ per ml) during chlorination of water (0.9 mg/L of residual chlorine)

Type	Strain	Virulence	$TCID_{50}$ after exposure (in minutes)							
			0	2 1/2	5	10	20	30	60	90
I	LSc, 2ab	attenuated	2.5×10^3	5	5	5	5	5	0	0
II	P-712,Ch,2ab	attenuated	5.0×10^3	16	16	10	10	5	5	5
III	Leon 12· $a_1{}^b$	attenuated	2.5×10^3	5	5	5	5	5	0	0
I	Mahoney	virulent	10.0×10^3	5	0	0	0	0	0	0
II	MEF-I	"	5.0×10^3	5	5	0	0	0	0	0
III	Saukett	"	16.0×10^3	5	5	5	0	0	0	0

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A higher resistance to chlorine of the attenuated than the virulent strains of poliomyelitis virus may be of interest in two respects:

a) It is quite possible that the newly discovered property of the attenuated strains is related to the genetic changes of their physiological and biochemical structure, such as changes in their ability of multiplication under high and low temperature and their reaction to the presence of bicarbonates in the medium. Should this be true, the above mentioned property could serve as a marker of the attenuation of the poliomyelitis virus. The data obtained point to necessity of searching similar new properties by comparative investigations of the effect of other various viricidal and viristatic substances on the attenuated and nonattenuated strains of poliomyelitis and possibly other kinds of viruses.

b) On the other hand, a higher resistance to chlorine of the vaccine strains obtained by A.B. Sabin may be of considerable advantage, as compared with the wild strains of virus, for the spread of the attenuated strains in nature (drinking water and sewage), which may be of epidemiological importance.

The spread of virus with sewage is necessarily connected with its final contact with the soil. Murphy (1958) has shown that the strain of type II poliomyelitis virus, Lansing, is adsorbed by particles of clay, especially by kaolin. A further study of the adsorption of various strains of poliomyelitis virus by different kinds of soil was of considerable interest.

In the present study preliminary data has been obtained concerning the adsorption of attenuated (LSc,2ab) and virulent (Lugovskoy) strains of I type poliomyelitis virus and a strain

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of ECHO 7a virus by sandy loam, loamy sand and peat which are the kinds of soil most often irrigated with sewage.

The samples of soils were first dried, ground and passed through a sieve, then samples of 10 g were placed into paper packages and sterilized in an autoclave The virus dilution (1:10) was prepared either in physiological saline or sewage and 20 ml.of it was added to 10 g. of sterile soil. After exposure for one hour the suspension was filtered through sterile filter paper and the concentration of the virus in the filtrate was determined by means of serial ten-fold dilutions and inoculation from each dilution of four tubes of monkey kidney cell cultures. Suspensions of virus in physiological saline or sewage without the addition of soil served as controls.

The pH was determined in the filtrates from the suspensions of various kinds of soils without the addition of the virus and it proved to be approximately from 5.5 (peat) to 6.6 (sandy loam). Then the virus was added to the filtrates and after standing for one hour the amount of it still present was determined. The fall of $Lg TCID_{50}$ per ml. as compared to that in the control never exceeded 0.5.

The results obtained show that peat soil gave very little adsorbtion of virus as the inconsiderable difference in the titers of virus in the test suspension and that in the control were statistically insignificant. All the virus strains under investigation were readily adsorbed by loamy sand and especially by the sandy loam(table 4). In these tests titers of the virus in the filtrates (lg. $TCID_{50}$ per ml.) fell by 2.0 to 5.0 lg., which proved that these kinds of soil possess a high absorbing

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capacity. The absorption process went to a greater extent in physiological saline than in sewage.

Table 4

Adsorption of attenuated and virulent strains of poliomyelitis and ECHO viruses by various types of soil. (Amount of virus absorbed by soil expressed in lg. $TCID_{50}$ per ml.) x)

Virus, strain	Serologic type	Virulence	Type of Soil		
			Peat	Loamy sand	Sandy loam
Polio LSc, 2ab	1	attenuated	1.00	4.00	5.00
Polio Lugovskoy	1	virulent	2.00	3.00	3.50
ECHO	7a	-	1.00	3.00	3.80

x) The experiments were carried out in physiological saline at pH 7.0 temperature $+4^{0}$ and exposure of virus to soil for 60 min.

In five tests out of six the vaccine strain of I type was adsorbed to a greater extent by the loamy sand and sandy loam than the nonattenuated strain of the same type of poliomyelitis virus.

If the adsorbent does not produce any viricidal effect the adsorbed virus in nature usually survives longer than the nonabsorbed. Consequently, one mays suppose that the greater absorption of the attenuated strain of poliomyelitis virus promotes its longer survival in nature as compared to the virulent

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strains, and provides a better spread of vaccine strains among the population.

A comparative study of the vaccine and virulent strains of poliomyelitis virus in respect to their sensitivity to chlorine and their adsorption by various kinds of soil reveals a new aspect of the profound changes occurring in the virus as result of the attenuation process.

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INSTITUTE FOR POLIOMYELITIS RESEARCH

STAT

INTERFERENCE BETWEEN NATURALLY OCCURRING (WILD) AND VACCINE POLIOVIRUS STRAINS IN THE HUMAN INTESTINAL TRACT

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Investigation of interaction between vaccine and naturally occurring (wild) polioviruses in the human intestinal tract is part of an extensive investigation program carried out under Prof. M.P.Chumakov's guidance by the Institute for Poliomyelitis Research, Academy of Medical Sciences of the U.S.S.R., during large-scale vaccination with live poliovirus vaccine from A.B.Sabin's strains (Chumakov, M.P., I960).

In the vaccination with live vaccine immunologic effect depends on the multiplication of the virus in the cells of the intestinal tract which reproduces natural latent infection. Study of the factors affecting this process in the intestinal tract is extremely important.

Interference between vaccine strains and spontaneous enteric viruses as well as between different types of vaccine viruses may present one of such factors.

Until recently phenomenon of interference between different types of polioviruses and other viruses in the intestinal tract has not been studied very extensively. Most of the data on interference between these viruses were obtained using different laboratory models - white mice and monkey (Jungeblut, I945, I948 a, b, Bodian, I949, Dömök, I957, I958, I959), chick embroys (Okuno, Kusumoto, Ishii, Sugai, I956), and tissue cultures (Ledinko, I953; Ledinko and Melnick, I954; Le Bouvier, I954; Jungeblut and Kodza, I959; Drake, I959).

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These extensive investigations resulted in the establishment of the capacity of different poliovirus types to interfere with each other, as well as with other viruses. It was shown that the outcome of this interaction depends on sequence and time of introduction of the first and the second of interfering viruses and on the dose of each.

Until recently, however, it was not known whether the established regularities are inherent in the natural process of interference occurring in the human intestinal tract[x].

Reports on isolation of two viruses from one stool specimen (Rhodes et al., 1950; Melnick, 1950, Dalldorf, 1951; Curnen and Melnick, 1951, Dalldorf, Albrecht, 1955; Chumakov, Drozdov, Ashmarina, Shirman, 1958) only showed the possibility of simultaneous presence of these viruses in the intestinal tract.

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x/ Numerous data available from the literature on microbial antagonism between representatives of enteric flora (Peretz, 1959, and others) can not serve as the basis for any analogy with viral interference. Similarity between these phenomena is merely superficial. In virus interference the process occurs in the host cell and is closely related with its condition. Bacterial antagonism in the intestinal tract occurs without direct participation of the cells of the body which distinguishes it qualitatively from interference between viruses.

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Introduction into practice of attenuated strains of poliomyelitis virus permitted investigation of the process of their interaction in the human intestinal tract. First observations (Sabin, I956, I957) already demonstrated the difference of this process from what had been observed under experimental conditions. Thus, it was found that type II poliovirus possesses greater capacity for interference compared to types I and III. Sabin's further studies (I959) showed that multiplication of type I vaccine virus in the intestinal tract may be prevented by adenoviruses type 2 and I6, ECHO-3, ECHO-7 and ECHO-9 viruses, Coxsackie A-7, A-11, B-2 and B-3 viruses. Besides, Sabin has discovered a new type of enterovirus multiplying only in human cells and capable to interfere with vaccine poliovirus. Studies by Gelfand et al.(I959), Paul et al.(I959), as well as considerable data accumulated by Benyesh-Melnick, Melnik and Ramos-Alvarez (I959) indicate that the phenomenon of interference between viruses in the intestinal tract is observed rather frequently and may have a significant influence of the process of vaccination with live poliovirus vaccine.

An exceptionally large scale of vaccinations with live poliovirus vaccine attained in the Soviet Union (Chumakov et al. I959, Chumakov, I960) makes the investigation of interference between vaccine and spontaneous enteric viruses particularly urgent because the knowledge of the peculiarities of this process will permit to achieve higher effectiveness of the vaccination.

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During live poliovirus vaccination program in Estonian SSR we studied some aspects of interaction both between vaccine and naturally occurring poliovirus strains and between different types of the vaccine virus.

Materials and Methods

The first part of the investigation (study of interaction between naturally occurring and vaccine polioviruses in the intestinal tract) was done on the material obtained from a children's institution (age of the children from 0 to 3 years) where aliquots of the original Sabin type I vaccine (strain LSc, 2ab) had been given.

The children received 100,000 TCD_{50} of the vaccine virus on a piece of bread or cake followed by the ingestion of water, and to younger children the virus was given in a spoonful of sweetened water or sugar syrup.

Stool specimens were collected at 23 days and the day before vaccinations and twice weekly during a month after vaccination.

10% suspensions by weight were prepared from stools, centrifuged at 4,500 rpm for 30 to 45 minutes, and the supernatant was treated with antibiotics. Tests for virus isolation were made in rhesus kidney cell tube cultures (primary inoculation and single passage for each specimen, additional passages when necessary).

When a virus was detected, its amount was determined by titrations in tube cultures of the same tissue cells. Each of 10-fold dilutions was inoculated into 4 tubes (0.2 ml per tube). 50% endpoint was calculated after Reed and Muench.

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Titration results presented in this paper are expressed as number of TCD_{50} per I gm of stools.

Virus isolates were typed with homotypic hyperimmune rabbit sera in tube tissue cultures or in bottle tissue cultures under agar (plaque method). Original stool suspensions or (when this was impossible) tissue culture fluids from primary cultures were used for typing.

Of I54 children surveyed before vaccination 40 (26 per cent) were carriers of cytopathogenic agents most of which belonged to type II poliovirus.

A few days before vaccination in this institution one of the children developed paralytic poliomyelitis caused by type II virus. This gives ground to believe that an epidemic, highly neurotropic strain of poliovirus was circulating in this community.

By now we have results of survey of I9 children from whom type II wild poliovirus was isolated before vaccination. Two of the children were not vaccinated but were in contact with the vaccinees.

The second part of the investigation (study of interaction between different types of vaccine polioviruses in the intestinal tract) was done on the material from an institution for children of 0 to 3 years of age.

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In the vaccination with monovaccines (Sabin's original strains) we shortened the interval between two feedings so that type II virus was administered at the height of type I virus multiplication in the intestinal tract. The procedure of vaccination was the same as in the first institution.

Stool specimens were collected the day before and twice weekly after the vaccination (up to 40 days). Blood specimens were taken prior to and 40 days after the first feeding.

The technique of virologic tests with feces is mentioned above. Titers of poliovirus antibody in serum specimens were determined by the cytopathogenic neutralization test in tube tissue cultures, the titer below I : 4 being considered zero.

R E S U L T S

I. Interaction between naturally occurring type II poliovirus and type I vaccine poliovirus

We observed two variants of interaction between naturally occurring and vaccine poliviruses.

a) Multiplication of naturally occurring virus in the intestinal tract before vaccination prevented vaccine virus multiplication.

Figs. I-4 present individual curves of fecal excretion of the virus in 4 children examined. On the abscissa time of survey (counted from the day of vaccination designated 0), and on the ordinate amount of the excreted virus are shown. Black columns designate type II virus, white columns - type I virus, shaded

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columns - mixture of types I and II. In a number of cases we were able to correlate the results obtained with data of serologie tests done by I.N.Dobrova. These data are shown in some of the figures by corresponding periods of tests.

Examination of the figures shows that after immunization the vaccine virus could not be detected in any of the stool specimens while the wild virus continued to be excreted extensively.

In the group of I7 vaccinated carriers of the naturally occurring (wild) virus no establishment of the vaccine virus was found in 5 (29 per cent). In the same institution 46 children without spontaneous virus carriage were examined, and all of them (I00,0 per cent) excreted the vaccine virus after immunization. The difference between these two groups in a relative number of persons susceptible to vaccine virus is statistically reliable.

Thus we established the occurrence of interference between type II wild poliovirus and type I vaccine virus in the human intestinal tract.

It is noteworthy that in all cases of interference prevaccination titers of naturally occuring viruses were high (above log $I0^{4.2}$ TCD_{50}). So the vaccination in these cases was very likely to coincide with a period of most extensive multiplication of the wild virus in the intestinal tract.

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b) Multiplication of naturally occurring virus before vaccination did not prevent the establishment and multiplication of the vaccine strain.

Such results we observed in I3 cases of I8 (a child, wild virus carrier, who received no vaccine but picked up the virus as a result of contact with the vaccinated is included into this group). The wild virus continued to be excreted at 2 to 6 days after vaccination. In no case was any prolonged combined excretion of the two viruses observed.

Did we have in these cases inhibition of the wild virus by the vaccine? To give a negative answer to this question would be possible if we could be certain that in all cases there was coincidence of the vaccination with cessation of type II virus multiplication in the intestinal tract. The likelihood of such a coincidence is very little. Accordingly, the cessation of the wild, virus excretion after ingestion and implantation of the vaccine virus may be regarded only as interference between type II wild virus and type I vaccine virus.

We observed that in the first variant of interaction between wild and vaccine viruses the amount of the wild virus excreted before vaccination was considerable (log $10^{4.2}$ - log $10^{6.0}$, the average log $10^{5.28}$ TCD_{50}) and in the second variant the amount of excreted virus was relatively small (log $10^{0.5}$ - log $W^{3.4}$, the average log $10^{2.3}$ TCD_{50}). Thus there exists a

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correlation between the amount of the wild virus excreted before vaccination and the results of virus interaction (see fig.5).

Most extensive excretion of the virus corresponds to the peak of intestinal infection. It is just in this period of its multiplication that the wild virus prevents the establishment of the vaccine virus. If the ingestion of the vaccine virus does not coincide with this phase, the reverse occurs - the vaccine virus establishes itself and eliminates the wild virus from the intestinal tract. Such an outcome of the interaction is possible prior or subsequent to the peak of the wild virus multiplication.

We had some reasons to define the duration of wild virus excretion before vaccination depending on its amount in the stool specimen collected 23 days prior to vaccination, and on immunologic indices. These data permit some judgement of the stage at which elimination of the wild virus from the intestinal tract was observed.

Fig.6-9 present cases in which we suppose the wild virus to have been inhibited early in its reproduction. Figs. I0-I4 show the elimination of the wild virus at the decline of its multiplication. Figs. I5 and I6 show the results of contact of virus carriers with children vaccinated with type I polivirus.

In order to find out whether there are any peculiarities

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in the excretion of the vaccine virus after it has elininated the wild one, we compared curves of vaccine virus excretion in two group of the vaccinated without type I poliovirus antibody. The first group consisted of 8 children excreting the wild virus before vaccination. The second (control) group consisted of I4 children without prevaccionation virus excretion (see fig.I7). Complete conformity of the compared curves indicates that previous carriage of the wild virus and interference phenomenon do not influence the pattern of type I vaccine virus multiplication in the intestinal tract.

Consequently, infection with naturally occurring type2 virus does not produce any marked refractoriness in the intestinal tract to subsequent infection with vaccine virus. It should be emphasized that we consider the intestinal tract as a whole and have no judgement of the refractoriness of individual cells or parts of the intestinal tract.

II. Interaction between type I and type II vaccine polioviruses

Children under observations were given type II virus 7 days after type I virus vaccination. As was shown by surveys in a comparable group of children (fig.I7), multiplication of type I vaccine virus is maximum 6-9 days after vaccination. Feeding with type II virus at the height of type I virus multiplication in the intestinal tract gave an opportunity to

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test the capacity of type I virus to protect the intestinal tract from infection with type II virus and, on the other hand, to find out the capacity of type II virus to interfere under such unfavourable conditions.

Most of the surveyed children excreted type I virus at 3 and 7 days after vaccination in considerable titers (fig.I8). Type II virus ingested at this time proved capable of implantation and extensive multiplication in the intestinal tract despite the previous infection of the latter with type I virus. The data presented below refer to I8 children in whom type I vaccine virus established in the intestinal tract and was excreted at 3 and 7 days after vaccination.

At 3 and 7 days after type II virus ingestion six children excreted this virus mixed with type I virus. Nine children excreted a mixture of the two viruses in the first stool specimen and only type II virus in the second specimen. Three children excreted only type II virus in both specimens (fig.I8, Table I).

Consequently, type II vaccine virus proved capable of not only implanting and multiplying in the intestinal tract, but also of inhibiting type I vaccine virus in the period of its extensive multiplication.

Data of serologic survey confirming these findings are presented in Table I. As is seen in the Table, rise of type II antibody titer was observed in all children and reached geometric means titer of $>$I58. Under the same circumstances rise of type I anti-

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body titer was observed only in 5 of I3 children (38 per cent) and reached geometric mean titer of 2 for the whole group. Antibody response does not depend on the exact time of cessation of type I virus excretion during the observation period. Different combinations of viruses excreted after feeding with type II virus may be regarded as a reflection of one and the same process of type I virus inhibition by type II virus occurring with different speed.

Thirty days after feeding with type I monovaccine homologous antibody develop in 76.4 per cent negative children (Chumakov et al. I959). Verlinde and Wilterdink (I959) observed antibody rise in I00 per cent of vaccinated in whom the vaccine virus was established. Geometric mean titer of type I antibody 30 days after vaccination of non-innune children is 30 and greater (Chumakov et al. I959).

Consequently, artificially shortened period of type I vaccine virus multiplication in the intestinal tract which we observed is not sufficient for complete antibody response.

Discussion

The results of our observations demonstrate the capacity of type II poliovirus (both naturally occurring and vaccine strains) to interfere with type I vaccine-virus.

There is a difference between naturally occurring and vaccine strains of type II poliovirus in their interference with

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type I vaccine virus. Type II wild virus established in the intestinal tract can inhibit type I vaccine virus only in the period of most extensive multiplication of the former (which in our observations corresponds to its fecal excretion in amounts of $IO^{4.2}$ TCD_{50} or greater). Type II vaccine virus inhibits type I vaccine virus not only at their simultaneous introduction in the intestinal tract, as Sabin (I959) reported (fig.I9), but even during most extensive multiplication of type I virus in the intestinal tract when conditions for implanation and multiplication of newly introduced virus are most unfavourable. This indicates a greater interfering capacity of type II vaccine virus compared to that of type II wild virus. It may be suggested that in the process of attenuation of type II poliovirus increase of interfering capacity goes parallel to decrease in neurovirulence.

As our observations demonstrated, interference between viruses in the intestinal tract may be the cause of failure of vaccinations in a number of cases, which was confirmed by Sabin's observations (I959).

Wide circulation of enteric viruses among population in summer months (60-70 per cent of virus carriers in some children institutions, according to our data) may lead to reduction in effectiveness of summer vaccinations with live poliovirus vaccine. Therefore it is most advisalbe to carry out vaccinations in winter months when enteric virus circulation is

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reduced considerably. But even under such circumstances revaccination is necessary to compensate for cases of vaccination failures due to interference.

Mass character of vaccinations also helps to compensate for occasional cases of vaccination failure. Long-range observations on immunologic responses in children vaccinated in institutions show (Chumakov, I960) that children who did not respond with antibody development one month after vaccination develop antibody later on (2-3 months after vaccination). In such cases immunization is provided by contact transmission of vaccine virus from the vaccinated excretors.

Interference phenomenon has already found practical application in poliomyelitis control. Use of type II monovaccine (Hale et al., I959) or trivaccine (Chumakov, I960) as a means for rapid interruption of poliomyelitis outbreaks caused by naturally occurring type I poliovirus is based on this phenomenon and has given encouraging results.

Conclusions

I. Occurrence of interference between naturally occurring type II poliovirus and type I vaccine virus in the human intestinal tract has been established.

2. The outcome of interference is influenced by the extent of the wild virus multiplication. At the height of its multiplication in the intestinal tract the wild virus prevents the implantation of the vaccine virus. At the initial and final

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stages of its multiplications in the intestinal tract the wild virus may be eliminated by the vaccine virus.

3. After elimination of the wild virus the vaccine virus multiplies in the same manner as in the intestinal tract of persons who were not virus carriers before vaccination.

4. Interference between viruses in the intestinal tract may by the cause of vaccination failure in a number of cases.

5. Type II vaccine virus has greater capacity for interference compared to that of naturally occurring type II virus and of type I vaccine virus.

6. The period of type I vaccine virus multiplication shortened by interference is not sufficient for development of complete immunity.

References

I. Chumakov, M.P. - On mass oral immunization of population in the Soviet Union against poliomyelitis with live vaccine, from A.B. Sabin's attenuated strains., Moscow, I960.

2. Jungeblut, C. - Journ. Exp. Med. I945, 8I, 275.

3. Jungeblut, C - Proc. Soc.Exp.Biol.Med. I948, 68, 3, 6I5.

4. Jungeblut, C. - Proc. Exp.Biol.Med. I948, 68, 9, I.

5. Bodian, D. - Amer.Journ.Hyg., I949, 49, 200

6. Dömök, J. - Acta microbiol. Hung., I957, 4, I83.

7. Dömök, J. - Acta microbiol Hung., I958, 5, III.

8. Dömök, J. - Acta virolog., I959, 3, 222.

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

9. Okuno, I. Kusumoto, K. Ishii, S., Sugai, T.,Med. Journ
Osaka Unir.1956, 6, 1003.

10. Ledinko, N. - Fed.Proc., 1953, 12, I, 451

11. Ledinko, N., Melnick, J., Journ.Exp.Med. 1954, 100, 247.

12. Le Bouvier, G., - Nature, 195 , 174, 4431, 649.

13. Sabin, A. - Science, 1954, 120, 3113, 357.

14. Jungeblut, C., Kodza H.,-Proc.Soc.Exp.Biol.Med., 1959, 102,
2, 270.

15. Drake J., - Virology, 1958, 6, I.

16. Rhodes, A., Clark, E., Knowles, D., Shimada, F.,Ritchie, R.,
Donohue, W., Armstrong, M., Wilson, F., McLean, N.,
Silverthorne, N., - Canad.Journ. Pub.Helath, 1950, 41, 173.

17. Melnick, J. , Bull. N.I. Acad.Sci., 1950, 26, 5, 342.

18. Dalldorf, G., - Journ.Exp.Med., 1951, 94, 65.

19. Curnen E., Melnick, J., - Pediatrics, 1951,8,237.

20. Dalldorf G., Albrecht, - Proc.Nat.Acad.Sci., 1955, 41, 978.

21. Chumakov, M.P., Drozdov, S.G., Ashmarina, E.E., Shirman G.M.
1958. A paper presented at a con -
ference in Riga, December, 1958.

22. Sabin, A.B. - JAMA. 1958, 162, 1589.

23. Sabin A., J A M A, 1957, 164, 1216.

24. Sabin A., in "Live poliovirus vaccines, U.S.A. Washington
1959, p.14.

25. Gelfand H., Potash L., Le Blanc D., Fox J., - Ibid.
p.203

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

26. Paul J., Horstmann, D., Riordan, J., Niederman, J., Goshicka I., Ibid, p. 2I8.

27. Benyesh-Melnick M., Melnick J., Ramos Alvanez M., Ibid.p.272.

28. Chumakov, M.P., Voroshilova, M.K., Vasil,eva, K.A., Bakina,M.N, Dobrova, I.N., Drozdov, S.G., Podsedlovsky, T.S., Kostina, K.A, Shirman, G.A., Yankevitch, O.D. Uspensky, J.S., Ashmarina,E.E. Problems of Virology, 1959, 5, 520.

29. Verlinde, J., Wilterdink, J., in "Live poliovirus vaccines", U.S.A., Washington, 1959, p.355.

30. Hale, J., Doraisingham, M. Lee, L., Kanagaratnam, K., Leong,K.W Monteiro, E., Ibid, p.280.

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Declassified in Part - Sanitized Copy Approved for Release @ 50-Yr 2014/05/08 : CIA-RDP81-01043R004800020001-2

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Table I. - Antibody response after vaccination with type I and type II poliovirus vaccine with weekly interval

Name	Antibody				Virus excretion after type II vaccination	
	One day before type I vaccination		40 days after type I vaccination			
	To type I	To type II	To type I	To type II	At 3 days	At 7 days
Tir.	0	0	0	I28		
Ani.	0	0	0			
Bol.	0	0	4	I024	Type I	Type I
Kru.	0	0	I6	5I2	+ Type II	+ Type II
Lep.	0	0	0	64		
Sco.	0	0	0	I28		
Hei.	0	0	0	64		
Lei.	0	0	0	I28	Type I	Type II
Pec.	0	0	0	5I2	+ Type II	
Pru.	0	0	0	32		
Sci.	0	0	I6	64		
Val.	0	0	4	256		
Ans.	0	0	8	256	Type II	Type II
Geometric mean titer			2	I58		
Ere.	I28	I6	I024	I28		
Kom.	5I2	I6	5I2	5I2	Type I + Type II	Type II
Naa.	64	0	2048	5I2		
Leh.	64	I6	5I2	I28		
Dud.	5I2	32	5I2	I28	Type II	Type II
Geometr. mean titer	I58	I0	794	200		

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Вакцинация вирусом полиомиелита I типа на фоне носительства II типа

Type I vaccination on the Background of type II virus carriage

Fig. 1

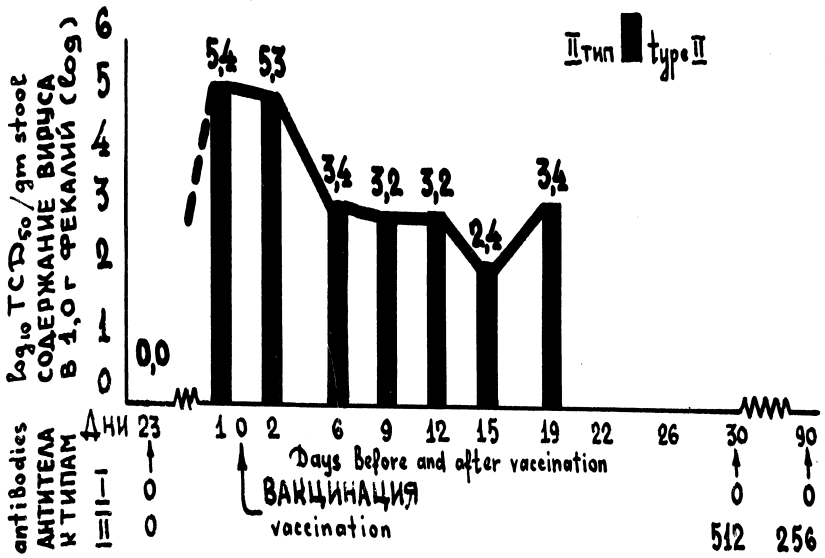
log10 TCD50/gm stool
СОДЕРЖАНИЕ ВИРУСА В 1,0г ФЕКАЛИЙ (log)
II тип type II
5,4 5,3 3,4 3,2 3,2 2,4 3,4
0,0
Дни 23 1 0 2 6 9 12 15 19 22 26 30 90
Days Before and after vaccination
antibodies АНТИТЕЛА К ТИПАМ
I 0 0 0
II 0 512 256
ВАКЦИНАЦИЯ
vaccination

Рис. 1.

Вакцинация вирусом полиомиелита I типа на фоне носительства II типа

Type I vaccination on the Background of type II virus carriage

Fig 2.

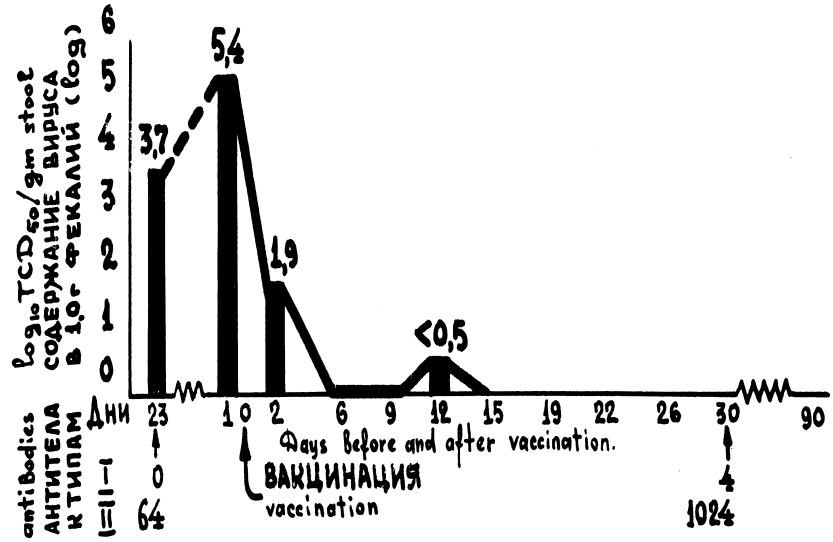
log10 TCD50/gm stool
СОДЕРЖАНИЕ ВИРУСА В 1,0г ФЕКАЛИЙ (log)
5,4 3,7 1,9 <0,5
Дни 23 1 0 2 6 9 12 15 19 22 26 30 90
Days Before and after vaccination.
antibodies АНТИТЕЛА К ТИПАМ
I 0 4
II 64 1024
ВАКЦИНАЦИЯ
vaccination

Рис. 2.

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ВАКЦИНАЦИЯ ВИРУСОМ ПОЛИОМИЕЛИТА I ТИПА
НА ФОНЕ НОСИТЕЛЬСТВА II ТИПА

Type I vaccination on the background of type II virus carriage Fig. 3.

Mik.

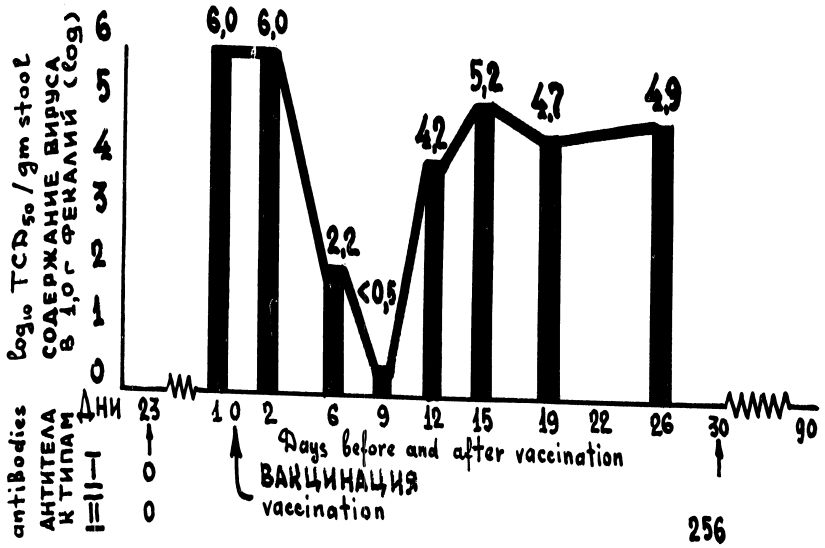
log10 TCD50/gm stool
СОДЕРЖАНИЕ ВИРУСА В 1,0 г ФЕКАЛИЙ (log)
6,0 6,0 2,2 <0,5 4,2 5,2 4,7 4,9
Дни 23 1 0 2 6 9 12 15 19 22 26 30 90
Days before and after vaccination
antibodies АНТИТЕЛА К ТИПАМ
I II I
0 0
ВАКЦИНАЦИЯ vaccination
256

Рис. 3.

ВАКЦИНАЦИЯ ВИРУСОМ ПОЛИОМИЕЛИТА I ТИПА
НА ФОНЕ НОСИТЕЛЬСТВА II ТИПА

Type I vaccination on the background of type II virus carriage. Fig. 4.

Vil.

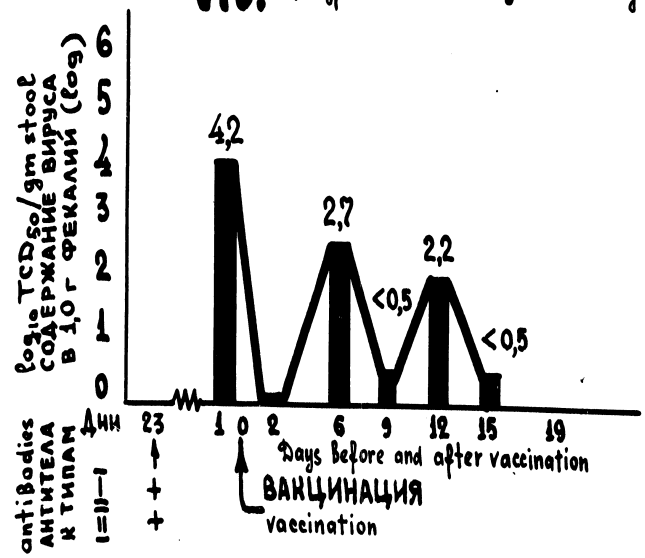
log10 TCD50/gm stool
СОДЕРЖАНИЕ ВИРУСА В 1,0 г ФЕКАЛИЙ (log)
4,2 2,7 <0,5 2,2 <0,5
Дни 23 1 0 2 6 9 12 15 19
Days before and after vaccination
antibodies АНТИТЕЛА К ТИПАМ
I II I
+ +
ВАКЦИНАЦИЯ vaccination

Рис. 4.

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Зависимость выделения вакцинного вируса полиомиелита I т. от предвакцинального размножения в кишечнике уличного вируса II т.

Relation of type I poliomyelitis vaccine virus excretion with prevaccination excretion of type II street virus

Fig. 5.

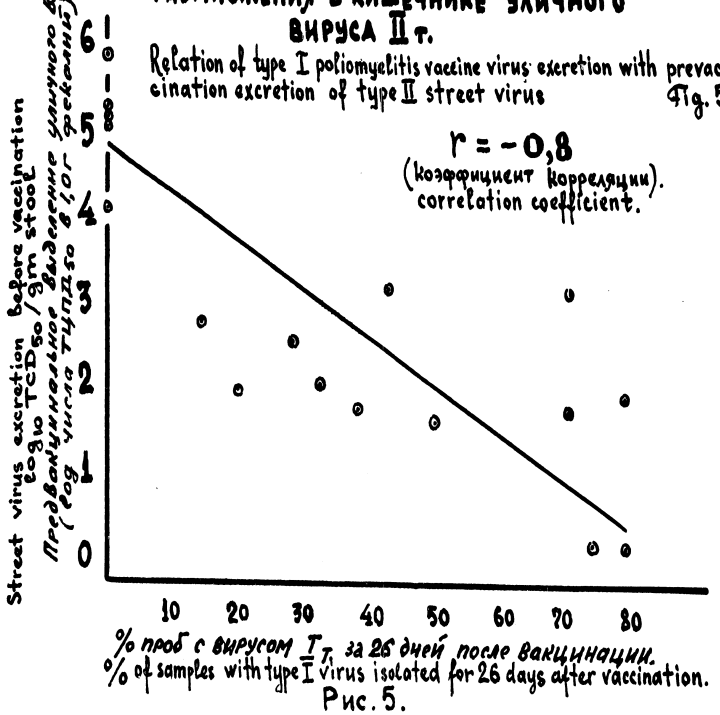

Рис. 5.

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Вакцинация вирусом полиомиелита I типа на фоне носительства II типа

Uuk.

Type I vaccination on the background of type II virus carriage

Fig. 6.

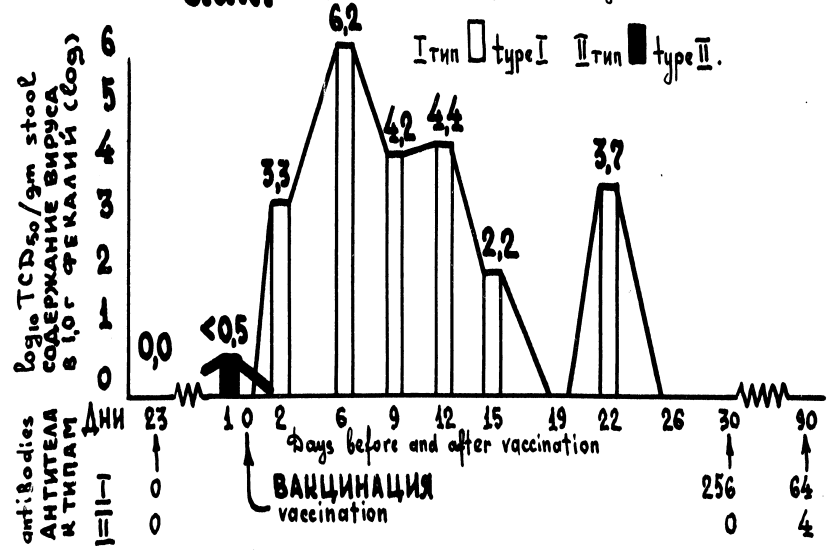

Рис. 6.

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Вакцинация вирусом полиомиелита I типа на фоне носительства II типа

Osi. Type I vaccination on the background of type II virus carriage Fig. 7.

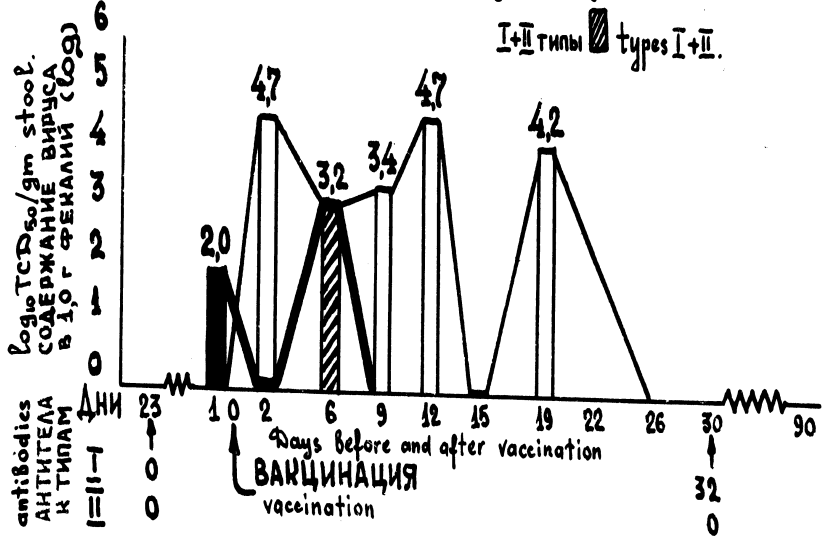

Рис. 7.

Вакцинация вирусом полиомиелита I типа на фоне носительства II типа

Pop. Type I vaccination on the background of type II virus carriage Fig. 8.

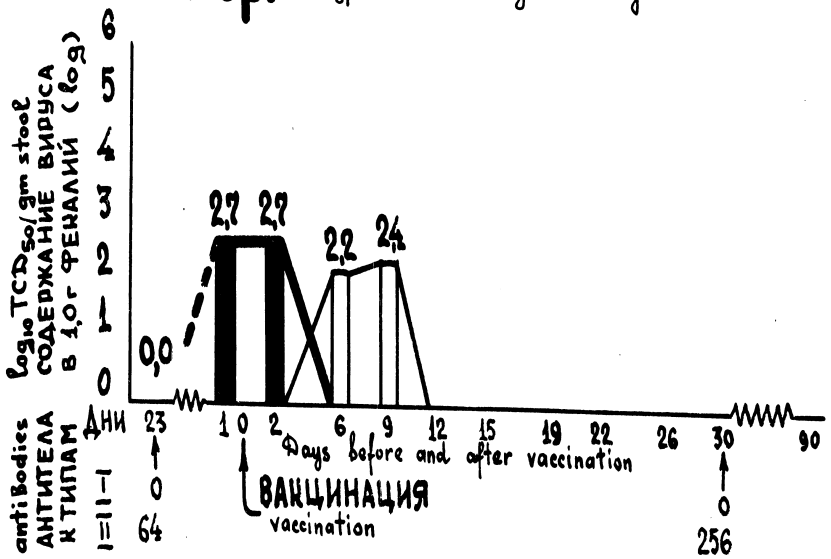
2,7 2,7
2,2 2,4
0,0
log10 TCD50/gm stool
СОДЕРЖАНИЕ ВИРУСА В 1,0 г ФЕКАЛИЙ (log)
0 1 2 3 4 5 6
Дни 23 1 0 2 6 9 12 15 19 22 26 30 90
Days before and after vaccination
antibodies АНТИТЕЛА К ТИПАМ I II I
0 64
ВАКЦИНАЦИЯ vaccination
0 256

Рис. 8.

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Вакцинация вирусом полиомиелита I типа на фоне носительства II типа

Saf. Type I vaccination on the Background of type II virus carriage Fig. 9.

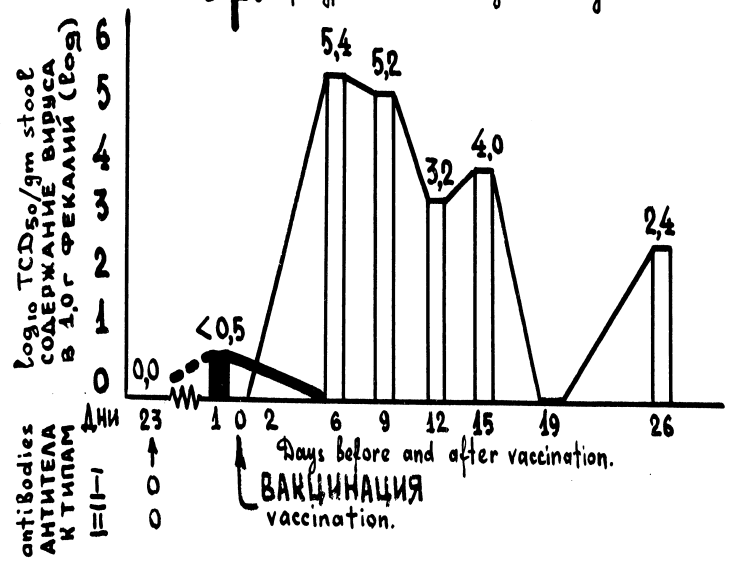

Рис. 9.

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Вакцинация вирусом полиомиелита I типа на фоне носительства II типа

Pot. Type I vaccination on the Background of type II virus carriage Fig. 10.

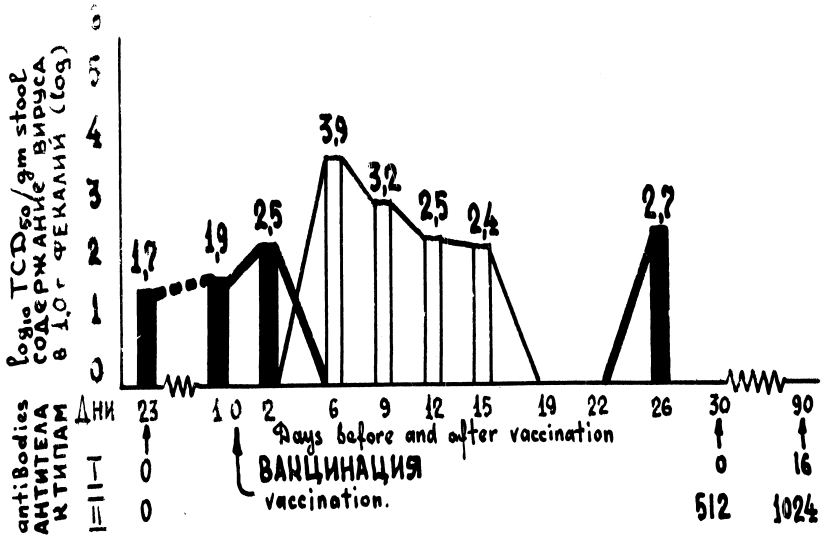

Рис. 10.

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Вакцинация вирусом полиомиелита I типа на фоне носительства II типа

Мее. Type I vaccination on the Background of type II virus carriage Fig. 11.

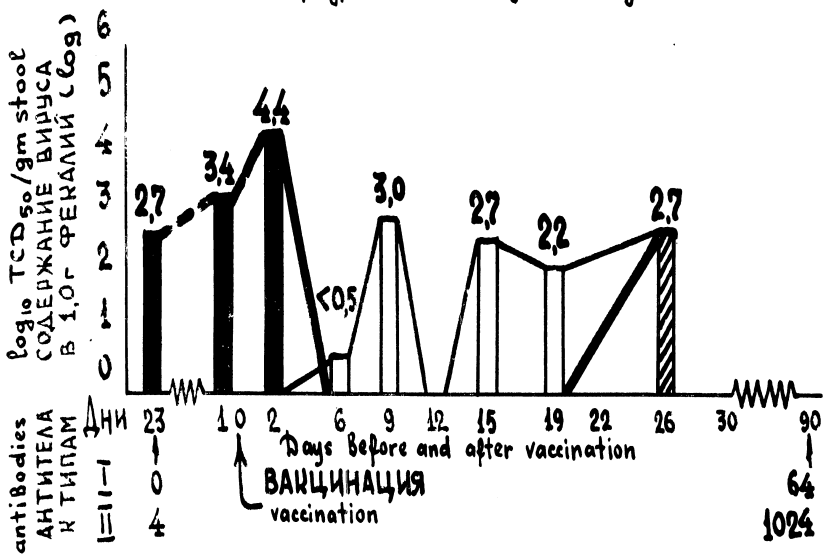

Рис. 11.

Вакцинация вирусом полиомиелита I типа на фоне носительства II типа

АБз. Type I vaccination on the Background of type II virus carriage Fig. 12.

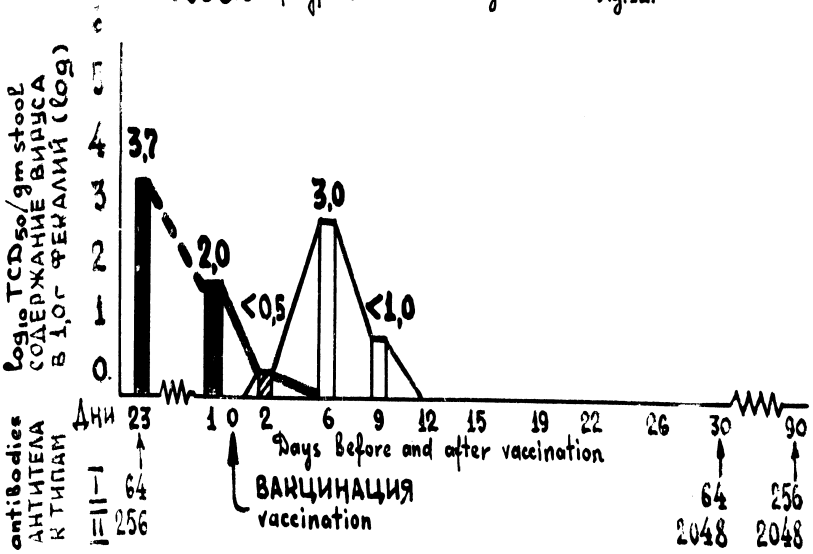

Рис. 12.

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Вакцинация вирусом полиомиелита I типа на фоне носительства II типа

Kur. Type I vaccination on the background of type II virus carriage Fig 13.

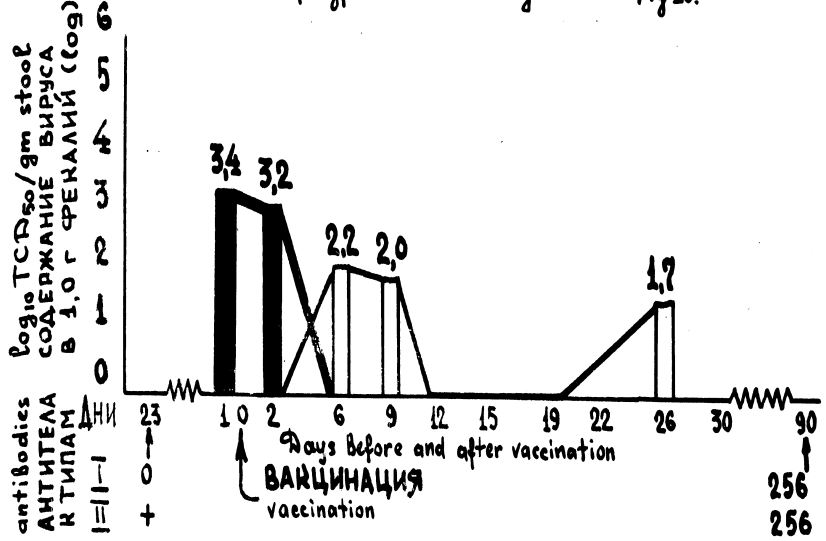

Рис. 13.

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Вакцинация вирусом полиомиелита I типа на фоне носительства II типа

Ško. Type I vaccination on the background of type II virus carriage Fig 14.

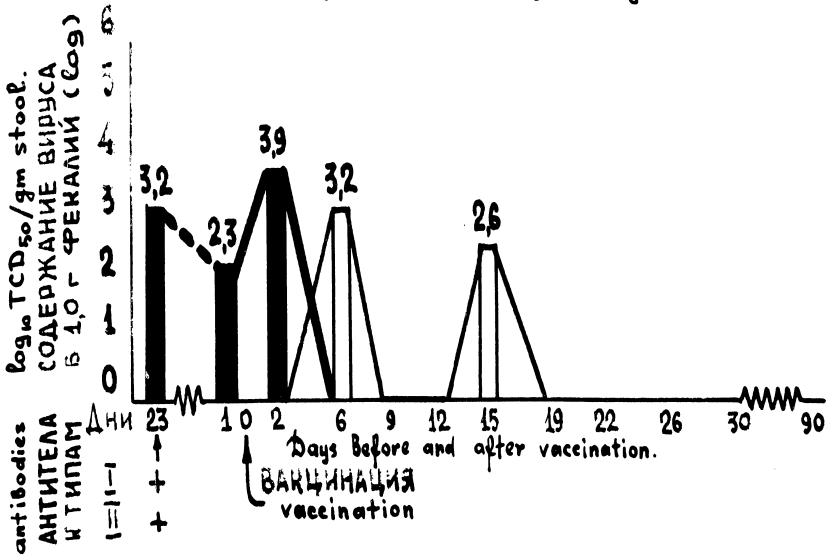

Рис. 14.

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Контакт с привитыми I типом вируса полиомиелита на фоне носительства II типа

Kra. Contact with type I vaccinee on the Background of type II virus carriage Fig. 15.

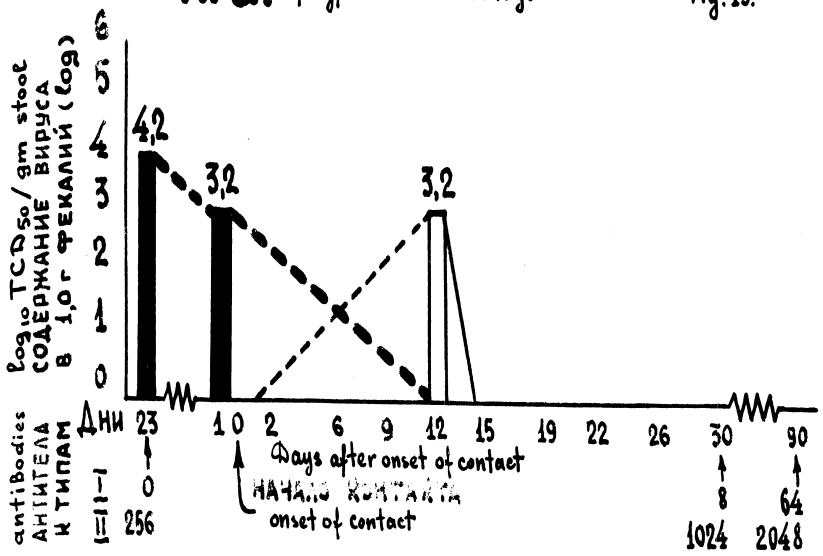
log10 TCD50/gm stool
СОДЕРЖАНИЕ ВИРУСА В 1,0 г ФЕКАЛИЙ (log)
0 1 2 3 4 5 6
4,2
3,2
3,2
Дни 23 1 0 2 6 9 12 15 19 22 26 30 90
Days after onset of contact
НАЧАЛО КОНТАКТА
onset of contact
antiBodies АНТИТЕЛА К ТИПАМ
I = 1-1 0 256
II = 8 64 1024 2048

Рис. 15.

Контакт с привитыми I типом вируса полиомиелита на фоне носительства II типа

Aub. Contact with type I vaccinee on the Background of type II virus carriage Fig. 16.

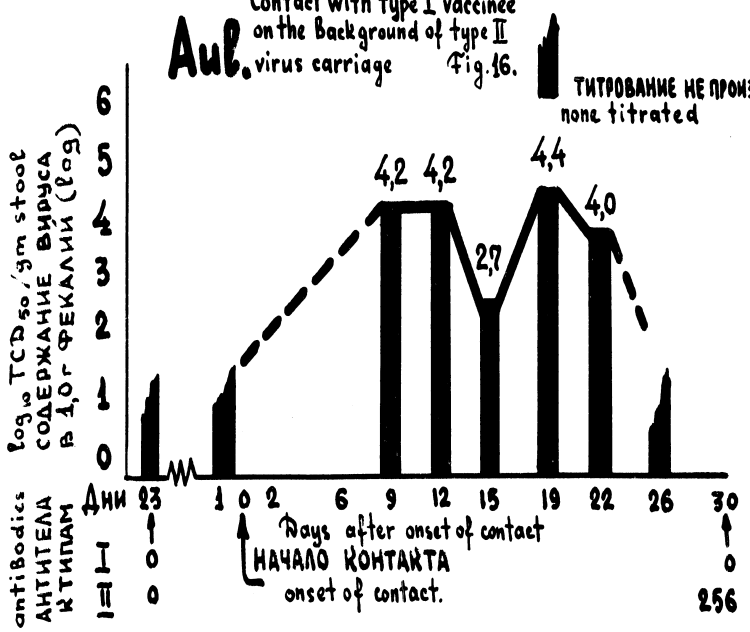

Рис. 16.

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Выделение вакцинного вируса полиомиелита I т.
у детей без антител к нему до вакцинации

Poliomyelitis type I virus excretion in type I antibody negative children before vaccination (average values)

(средние показатели)

Fig. 17.

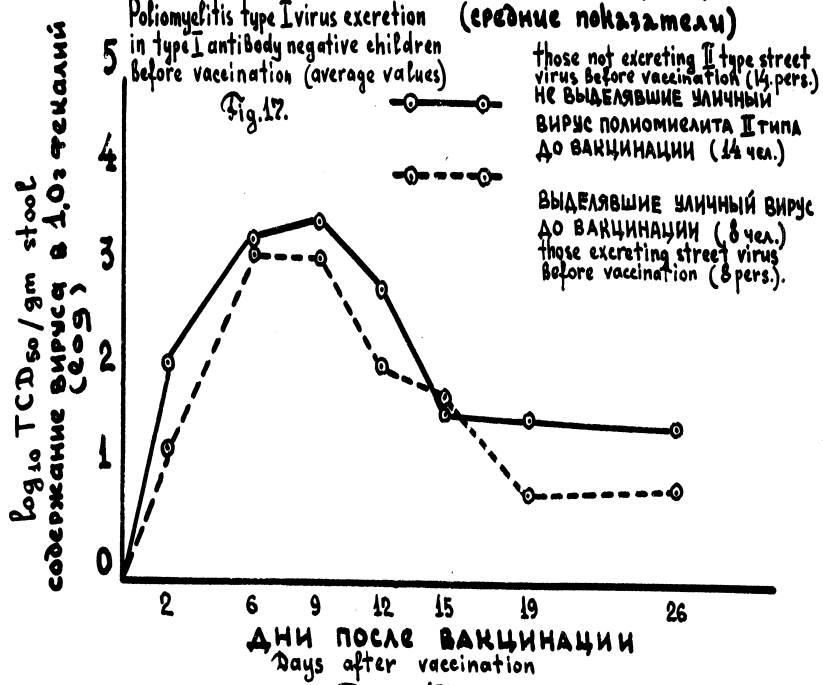

Рис. 17.

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Вакцинация вирусом полиомиелита II т. на высоте выделения вакцинного вируса полиомиелита I т.

Type II poliomyelitis virus vaccination at the maximum exeretion of type I poliomyelitis vaccine virus. Fig 18.

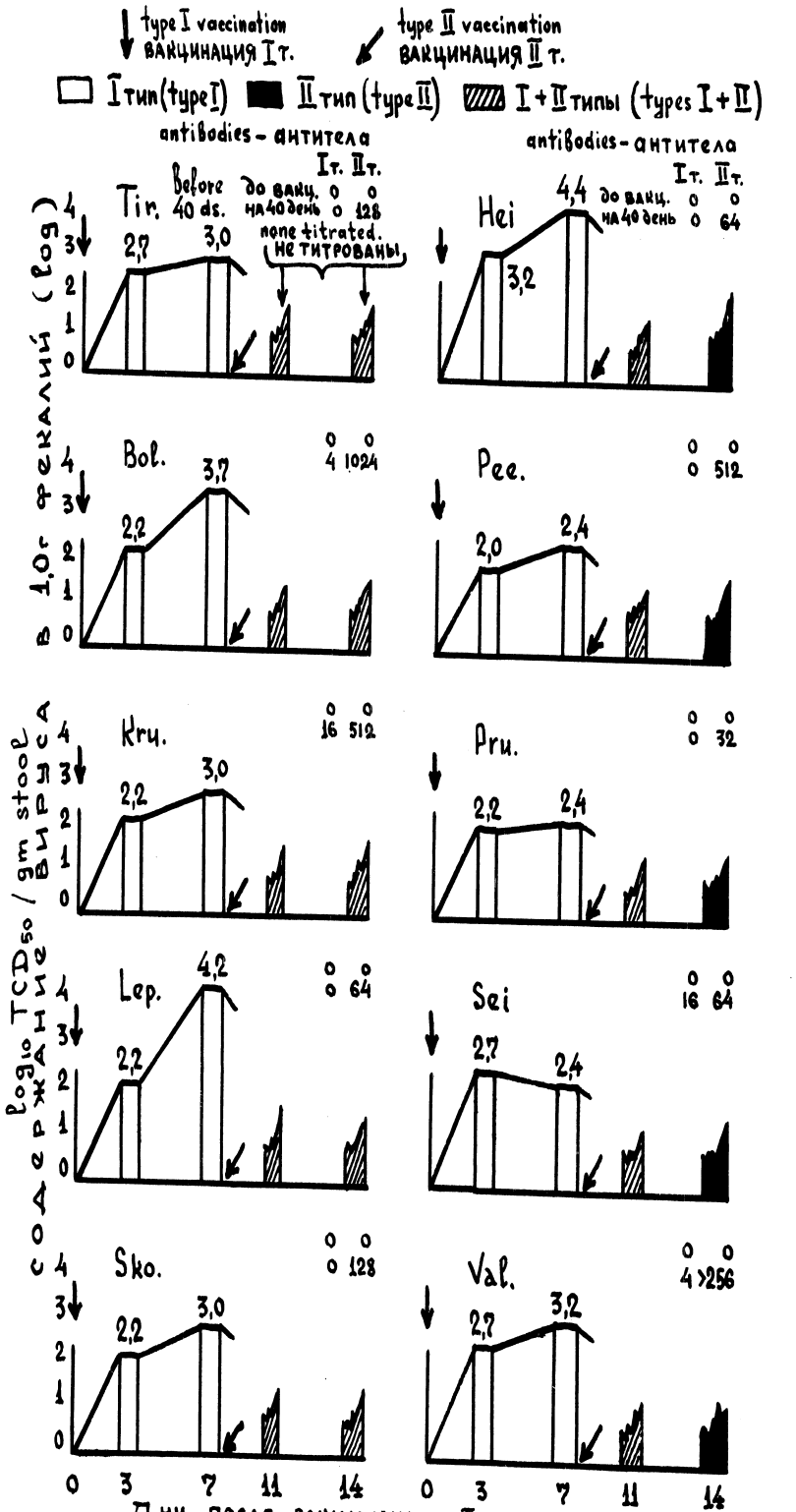

Рис. 18.

1265/1266

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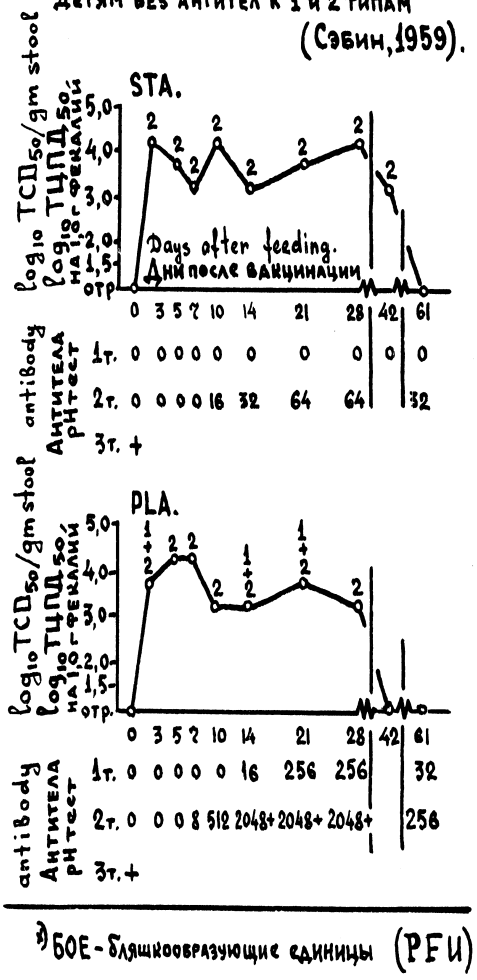
Результат скармливания смеси
1 и 2 типов полиовирусной вакцины
(по $10^{5,6}$ БОЕ*) штаммов LSc,2ab и P712,Ch,2ab)
детям без антител к 1 и 2 типам
(Сэбин, 1959).



*) БОЕ - бляшкообразующие единицы (PFU)

Рис. 19.

Effect of feeding mixture of type I and type II poliovirus vaccine strains ($10^{5,6}$ PFU each of LSc,2ab and P712,Ch,2ab to young adults without antibody for both of these types (Sabin, 1959) Fig. 19.

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The Spread of Polioviruses in the Population Vaccinated with the Live Attenuated Polioviruses in Comparison with the Nonvaccinated Population

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From the Hygiene and Epidemiological Stations of Liberec and Jihlava,
and from the Virus Department of Institute of Sera and Vaccines, Prague

In connection with the controlled field trial with live poliovirus vaccine in Czechoslovakia in 1958/59

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x) in collaboration with J. Kásová /Olomouc/, V.Potuznik /Budejovice/, D. Rezácová /Praha/, M. Suchánek /Ostrava/, J. Stastna /Usti/, M.Tarabcák /Kosice/ and J.Valihrach (Uherské Hradiste/.

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repeated investigations of the spread of enteroviruses in the vaccinated and nonvaccinated population were made before and after the vaccination of the children with live attenuated polioviruses (Sabin).

This paper presents the results of these investigations made in the period from November 1958 to October 1959.

Material and Methods

In the investigated populations stool specimens were tested for the presence of enteroviruses; the specimens being taken from healthy persons at random, predominantly from children up to the age of 10, partly also from older individuals.

The samplings were done in 4 Czech regions (Liberec, Jihlava, Ústi and Ostrava), in which the children were vaccinated with the three types of attenuated polioviruses and simultaneously also in control regions, in which live poliovaccine had not been used, in the period from December 1958 to February 1959.

In the individual sampling at least 120, but usually even more, of stool specimens were taken in each region, mostly from children institutions (creches, kindergartens,

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nurseries and boarding-schools). From one community only 2 stool specimens were taken maximally, the material was collected in many institutions of the whole region, proportionally to the density of the population.

The time periods in which the individual samplings were made are given in the tables and figures showing the results of the investigations.

The isolation of the viruses was performed from the 10% extract of faeces and 3 tube tissue cultures from monkey kidney cells were inoculated with 0.2 ml of suspension per tube. The isolated cytopathogenic agents were tested against three polio antisera by the current methods used in our Czechoslovac reference laboratory for enteroviruses; the identification of non-polioviruses have not yet been finished.

Results and Conclusions

Figure 1 reviews the results of the investigation of polioviruses spread in all the surveyed regions. The time of sampling is shown in the left lower corner of the figure.

More detailed results of the recovery of enteroviruses from vaccinated and non-vaccinated children in the

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regions in which live vaccine was used, are given in table 1. The analogically arranged results of the spread of viruses in the unvaccinated regions are presented in table 2.

From these tables it is possible to see that before the beginning of vaccination with live poliovirus vaccine no polioviruses were isolated in the region of Liberec, and in the second vaccinated region (Jihlava) two strains of type 1 were recovered.

After feeding a part of the child population with attenuated virus type 1 in December 1958 and type 3 in January 1959, we were able to isolate a great number of type 3 strains in the period of about 14 days after the feeding of type 3 and 1/2 month after feeding the children with type 1, but already in this short period after the mass introduction of the viruses into the population, type 1 virus was isolated in a very small number of children.

In the next sampling carried out already after vaccination with all three types of attenuated polioviruses in the period of approximately two months after feeding with type 2, three months after type 3 and four months after

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feeding the children with type 1, no type 1 strain could be found in a relatively large number of stool specimens tested from the vaccinated population, while viruses of type 2 and 3 occured more frequently, mostly in nonvaccinated children.

After the 1 and 1/2 to 2 and 1/2 months we could not isolate any type 1 strain in the sampling carried out around June 1959; one type 3 strain was recovered from a vaccinated child and only type 2 viruses occured in a greater number in this period.

In the further sampling performed on the peak of the season (September - October 1959), no strains type 1 and 3 were isolated in the vaccinated regions and only two strains type 2 could be found. When calculating the number of isolated type 2 strains to 100 investigated stool specimens we can see that, in comparison with the occurence of polioviruses in the control regions which were not vaccinated, the percentage of isolated type 2 viruses is very low and does not significantly differ from the occurence of type 2 in the population of unvaccinated regions, from which on the other hand we were able to isolate a number of type 1 and 3 strains.

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From the above mentioned results it is possible to suggest that after feeding a part of the child population with type 1 and 3 polioviruses, these viruses did not persist in the vaccinated population for a long time; on the contrary it can be regarded as probable that after a relatively short time these types of polioviruses not only disappeared from the population but could also influence the spreading on naturally occuring type 1 and 3 polioviruses in the vaccinated population.

Only type 2 of attenuated poliovirus administered as the last one seemed to persist in the population for a longer period. The number of isolated type 2 strains is, however, relatively very low and does not significantly exceed the percentage of the incidence of this type of virus in the population of the control regions, in which the children were not vaccinated with the live poliovirus vaccine. It is clear that no mass spread of type 2 poliovirus occured in the vaccinated population, all the more so, as we cannot exclude that both strains isolated in one vaccinated region (Jihlava) are wild, naturally occuring viruses introduced into the population from elsewhere.

On table 3, summarizing the results of investigations

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carried out in the vaccinated and control regions, we can see that on the peak of the season, i.e. in the fifth sampling carried out in September - October 1959 there was a higher incidence of type 1 and 3 polioviruses in the Czech control unvaccinated regions than in the regions where the children were fed. The possible objection that the attenuated polioviruses type 1 and 3 penetrated to the more susceptible population of the neighbouring control regions and persisted there for a longer time, does not seem to be justified. We believe this because:

a) we were not able to prove the spread of individual types of polioviruses in the Czech control regions, which closely communicate with the vaccinated regions, in the investigated samplings up to June 1959, and

b) the greatest part of polioviruses isolated in the control regions in September - October 1959 comes from the region of Gottwaldov, which is neighbouring to Slovak regions of Zilina and Bratislava. As can be seen on table 2 there was a high spread of polioviruses in Slovakia in the summer 1959 and it can therefore be supposed that 5 type 3 and 2 type 2 strains recovered in the fifth sampling in the region of Gottwaldov comes rather from the neighbouring Slovakia than from Czech regions in which the children were vaccinated with live poliovaccine.

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The Spread of Polioviruses in the Vaccinated (with live Polio Vaccine) and Unvaccinated Population of Czechoslovakia

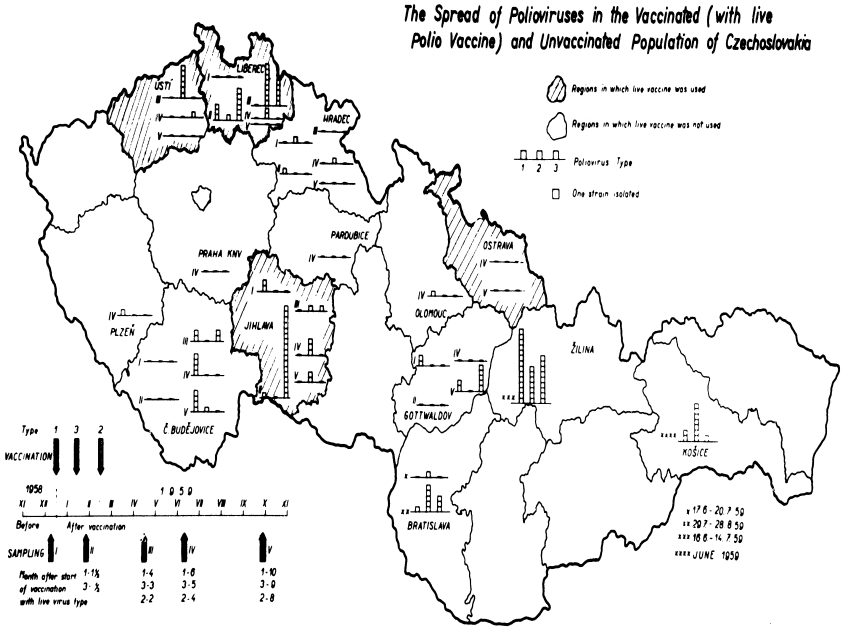

FIG.1

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Table 1

The Occurence of Enteroviruses in the Population of Czech Regions in which Live Poliovirus Vaccine was Used

Vaccinated regions	Live polio vaccine used	Sampling	Data of sampling	Months after start of vaccination	No of stool specimens tested	No of isolated viruses: Polioviruses: Total	Type 1	Type 2	Type 3	Others
Liberec	yes	I	27.XI.-14.XII. 1958.	Before	123	0 +/	0	0	0	1
	yes	II	23.I.-29.I.59	1 1/2	130	9/1	3/0	0/1	6/0	2/0
		III	10.IV-22.IV.	4	242	6/7	0	3/5	3/2	0/2
		IV	25.V-10.VI	5 1/2	193	0/2	0	0/2	0	0/1
		V	24.IX-5/X	9 1/2	150	0	0	0	0	0/2
Jihlava	yes	I	2.-11.XII 58	Before	119	2	2	0	0	5
		II	23.-31.I. 1959	1 1/2	115	11/7	0/1	0	11/6	0
		III	11.-20.IV	4	121	1/7	0	1/0	0/1	0
		IV	21.V.-9.VI	5 1/2	149	1/2	0	1/2	0	1/0
		V	30.IX.-10.X	9 1/2	188	0/2	0	0/2	0	4/11
Ústí n/L.	yes	I			Not done					
		II			Not done					
		III	9.IV-4.V.59	4	193	6/2	0	4/2	2/0	1/1
		IV	25.V.-5.VI	5 1/2	213	1/0	0	0	1/0	0/4
		V	1.-8/X.	9 1/2	111	0	0	0	0	0
Ostrava	yes	I			Not done					
		II			Not done					
		III			Not done					
		IV	24.VI.-7.VII	6 1/2	131	0	0	0	0	0
		V	12.-22.X	10	142	0	0	0	0	0/5

+/ Nominator: of isolated strains of viruses from the vaccinated persons.
Demominator: of isolated strains of viruses from the unvaccinated persons.

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Table 2

Spread of Enteroviruses in the Population of Czechoslovak Regions in which Live Poliovirus Vaccine Was Not Used

Region	Sampling	Date of sampling	N° of stool specimens tested	N° of isolated viruses				
				Polioviruses				
				Total	Type 1	Type 2	Type 3	Others
Hradec	1	5.-15.XII. 1958	III	1	0	1	0	3
	II	10.-11.II. 1959	93	1	1	0	0	0
	III	22.29.IV.	90	0	0	0	0	4
	IV	3.-5.VI.	174	1	0	1	0	6
	V	1.-20.X.	130	0	0	0	0	0
C.Budejovice	1	December 1958	91	0	0	0	0	1
	II	February 1959	30	0	0	0	0	0
	III	April	161	4	2	0	2	5
	IV	3.-26.VI.	219	4	4	0	0	2
	V	10.X.-20.XI	180	5	4	1	0	11
Gottwaldov	I	December 1958	91	2	2	0	0	4
	II	10.-21.11. 1959	120	0	0	0	0	0
	III					Not done		
	IV	25.V.-11.VI	230	0	0	0	0	5
	V	22.IX.-30/IX	129	7	2	0	5	2
Pardubice	I-III					Not done		
	IV	12.-22.VI. 1959	118	0	0	0	0	5
Praha KNV	I-III					Not done		
	IV	22.-29.VI 1959	127	0	0	0	0	2
Plzen	I-III					Not done		
	IV	2.VI.1959	112	1	1	0	0	3
Olomouc	I-III					Not done		
	IV	16.VI.1959	115	1	1	0	0	9
Bratislava (Slovakia)	x)	17.VI.-20/VII 1959	173	1	0	1	0	22
	xx)	29.VII-28/VIII	154	9	1	5	3	32
Zilin (Slovakia)	xxx)	16.VI.-14.VII. 1959	206	31+)	14	7	9	9
Kosice (Slovakia)	xxxx)	June 1959	101	10	2	7	1	3

+) mixture of polio and other virus.

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Table 3

The Spread of Enteroviruses in the Vaccinated (with Live Polioviruses/ and Unvaccinated Population of Czech Regions

Region	Live polio vaccine used	Sampling	Months after start of vaccination	Stool specimens tested No.	From vacc. / unvacc. persons	Polio type 1 No.	Polio type 1 per cent	Polio type 2 No.	Polio type 2 Per cent	Polio type 3 No.	Polio type 3 Per cent	Others No.	Others Per cent
Liberec	yes	I	Before	242		2	0.8	0	0	0	0	6	2.5
Jihlava													
Liberec	yes	II	1 1/2	245	47	3	6.58	1	0.05	17	36.17	2	0.82
Jihlava					198	1	0.5	1	0.5	6	3.03	0	0
Liberec	yes	III	4	556	106	0	0	8	7.5	5	4.7	1	0.9
Jihlava					450			7	1.6	3	0.3	3	0.7
Ústí m/L.													
Liberec	yes	IV	5 1/2	686	140	0	0	1	0.7	1	0.7	1	0.7
Juhlava					546	0	0	4	0.7	0	0	9	1.6
Ústí n/L.													
Ostrava													
Liberec	yes	V	9 1/2	591	140	0	0	0	0	0	0	4	2.8
Jihlava					451	0	0	2	0.4	0	0	18	4.0
Ústí n/L.													
Ostrava													
Hradec C.Budejovice Gottwaldov	not	I		293		2	0.7	1	0.3	0	0	8	2.7
Hradec Gottwaldov C.Budejovice	not	II		243		1	0.4	0	0	0	0	0	0
Hradec C.Budejovice	not	III		251		2	0.8	0	0	2	0.8	9	3.6
Hradec C.Budejovice Gottwaldov Pardubice Praha KNV Plzen Olomouc	not	IV		1095		6	0.5	1	0.1	0	0	32	2.9
Hradec C.Budejovice Gottwaldov	not	V		439		6	1.4	1	0.2	5	1.1	13	3.0

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A morphological study of the cells infected with attenuated and virulent strains of poliovirus. Electron and luminiscent microscopy

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1. With the help of fluorescent antibody specific antigen could be observed in monkey kidney and heart cell cultures 5-6 hours after inoculation. At first the specific antigen was localized in the cytoplasm of the cell. However, 18-20 hours later the specific antigen appeared in t the nuclear membrane and, 70 hours later, in the nucleus. By this time fluorescence of cytoplasm became less intensive. The kinetics of specific antigen accumulation in the cells occured simultaneously with the increase of the virus titer.

2. The accumulation of poliovirus in tissue culture cells was studied in the electron microscope SEM2-2.
   a) For this purpose a special method was developed for preliminary selection and orientation of the affected cells in phasocontrast microscope;
   b) comparative studies of the submicroscopic structural occurring in monkey heart heart cell cultures, induced by virulent and attenuated strains of poliovirus during the degeneration process, were carried out. Characteristic changes were detected in ergastoplasm, mitochondria, nuclear membrane, nucleus and nucleolus. The osmiofilic particles found in the cytoplasm were interpreted as poliovirus.

3. In order to study the relationship between the virus and the cell electron microscopic observations of the ultra-epithelial thin section of the intestinal cells of animals susceptible to the poliovirus (Cotton rats - "Sigmodon hispi-

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dus", monkeys - Macacus rhesus") were conducted. Ultra-thin sections were made on the ultramicrotome designed by Porter-Blum and were studied by means of electron-microscope SEM2-2.

a) The surface of the epithelial cells (striated board) is made of a specific organoid, which consists of the microvilli with a specific internal structure which provides the ingestion of the food substances from the digestive tract. It is suggested that the process of the intestinal viruses takes place on these surfaces of the microvilli. The submicroscopical structure of the cytoplasm of intestinal epithelial cells is a system of the membranes containing Palade's granules, tubules and reservoirs of ergastoplasm. The virus particles and the Palade's granules contain RNA which are of similar size. Thus, it is necessary to use a new method for differentiation of virus particles and granules in the cytoplasm of the cells free of virus.

b) The difference of the electron microscopical density (light and dark spots) of the intestinal epithelial cells is related with following vital activities:
   1) the ingestion (columnar or main cells), and
   2) the secretion (the goblet cells).

The possible ways of penetration of the virus into the cell and its excretion into the lumen of the digestive tract are discussed.

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4. The submicroscopical changes were observed in the ergastoplasm, the nuclear membrane, the nucleolus and mitochondria of the intestinal epithelial cells in animals infected with the poliovirus.

5. A comparative analysis of the changes occurring in the intestinal cells of the animals and in the cells of the tissue culture under the influence of the poliovirus are given in this report.

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